MEMORANDUM OF UNDERSTANDING ADDRESSING CERTAIN DISTRIBUTIONS OF COMPOUNDED HUMAN DRUG PRODUCTS BETWEEN THE [insert STATE BOARD OF PHARMACY OR OTHER APPROPRIATE STATE AGENCY] AND THE U.S. FOOD AND DRUG ADMINISTRATION

I. PURPOSE

This Memorandum of Understanding (MOU) establishes an agreement between the [insert State Board of Pharmacy or other appropriate State agency] and the U.S. Food and Drug Administration (FDA) regarding the distribution of inordinate amounts of compounded human drug products interstate[1] and the appropriate investigation by the [insert State Board of Pharmacy or other appropriate State agency] of complaints relating to human drug products compounded in [insert State] and distributed outside such State.[2] This is the MOU provided for by section 503A(b)(3)(B)(i) of the Federal Food, Drug, and Cosmetic Act (the FD&C Act) (21 U.S.C. 353a), and does not apply to veterinary drug products, biological products subject to licensure under section 351 of the Public Health Service Act (42 U.S.C. 262), and drugs that are compounded by outsourcing facilities under section 503B of the FD&C Act.

II. BACKGROUND

a. Section 503A of the FD&C Act describes the conditions that must be satisfied for human drug products compounded by a licensed pharmacist or licensed physician to be exempt from three sections of the FD&C Act requiring:

    1. Compliance with current good manufacturing practice (section 501(a)(2)(B) (21 U.S.C. 351(a)(2)(B));

[1] For purposes of this MOU, see the definitions of "inordinate amounts" and "distribution of compounded human drug products interstate" (also referred to as "distributed interstate") in Appendix A.

[2] As described herein, the State Board of Pharmacy or other appropriate State agency signatory is agreeing to take certain actions as described in Section III below. For example, if a State Board of Pharmacy signs the MOU, the State Board of Pharmacy agrees to take the actions described in Section III below with respect to drugs compounded by pharmacies in that State; in addition, the State Board of Pharmacy agrees that if it receives information about complaints or becomes aware of information about drugs compounded by physicians in the State and distributed interstate, it will forward the information to FDA and the appropriate State regulator of physicians as described in Section III.

2. Labeling with adequate directions for use (section 502(f)(1) (21 U.S.C. 352(f)(1)); and

3. FDA approval prior to marketing (section 505 (21 U.S.C. 355)).

b. To qualify for these exemptions, a compounded human drug product must, among other things,[3] meet the conditions in section 503A(b)(3)(B) of the FD&C Act, under which the drug product is compounded in a State that:

1. Has entered into an MOU with FDA that 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 (section 503A(b)(3)(B)(i)); or

2. Has not entered into an MOU with FDA 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 (section 503A(b)(3)(B)(ii)).

c. Section 503A(b)(3) of the FD&C Act directs FDA to develop a standard MOU, in consultation with the National Association of Boards of Pharmacy (NABP), for use by the States in complying with section 503A(b)(3)(B)(i). This MOU is the standard MOU developed by FDA for this purpose.

III. SUBSTANCE OF AGREEMENT

a. Investigation of Complaints Relating to Compounded Human Drug Products Distributed Outside the State

1. The [insert State Board of Pharmacy or other appropriate State agency] will investigate complaints of adverse drug experiences and product quality issues[4] relating to human drug products compounded at a pharmacy in [insert State] and distributed outside the State. Any investigations will be performed pursuant to the [insert State Board of Pharmacy or other appropriate State agency]'s established investigatory policies and procedures, including those related to prioritizing complaints, provided they are not in conflict with the terms of this MOU.

[3] To qualify for the exemptions under section 503A, a compounder must obtain a prescription for an individually identified patient (section 503A(a) of the FD&C Act). This MOU does not alter this condition.
[4] For purposes of this MOU, see the definitions of "adverse drug experience" and "product quality issue" in Appendix A.

2. Any investigations performed by the [insert State Board of Pharmacy or other appropriate State agency] under this MOU will include taking steps to assess (1) whether there is a public health risk associated with the compounded drug product; and (2) whether any public health risk associated with the product is adequately contained.

3. After the [insert State Board of Pharmacy or other appropriate State agency]'s investigation, if the complaint is substantiated, the [insert State Board of Pharmacy or other appropriate State agency], in accordance with and as permitted by State law, will take the action that the [insert State Board of Pharmacy or other appropriate State agency] considers to be appropriate and warranted to ensure that the relevant pharmacy investigates the root cause of the problem that is the subject of the complaint and undertakes sufficient corrective action to address any identified public health risk relating to the problem, including the risk that future similar problems may occur.

4. The [insert State Board of Pharmacy or other appropriate State agency] will maintain records of the complaint about adverse drug experiences or product quality issues relating to human drug products compounded at a pharmacy, the investigation of the complaint, and any response to or action taken as a result of the complaint, beginning when the [insert State Board of Pharmacy or other appropriate State agency] receives notice of the complaint. The [insert State Board of Pharmacy or other appropriate State agency] will maintain these records for at least 3 years. The 3-year period begins on the date of final action on a complaint, or the date of a decision that the complaint requires no action.

5. As soon as possible, but no later than 5 business days after receiving a complaint involving a serious adverse drug experience or serious product quality issue relating to a drug product compounded at a pharmacy and distributed outside the State, the [insert State Board of Pharmacy or other appropriate State agency] will, by submission to an Information Sharing Network[5] or by email to StateMOU@fda.hhs.gov, provide FDA with the information described in the Submission and Disclosure of Information section of this MOU (section III.c.1.a.i-iii).[6]

[5] For purposes of this MOU, see the definitions of "serious adverse drug experience," "serious product quality issue," and "Information Sharing Network" in Appendix A.

[6] The information includes the following: (i) Name and contact information of the complainant, if available; (ii) Name and address of the pharmacy that is the subject of the complaint; and (iii) Description of the complaint, including a description of any compounded human drug product that is the subject of the complaint.

6. After the [insert State Board of Pharmacy or other appropriate State agency] concludes its investigation of a complaint assessed to involve a serious adverse drug experience or serious product quality issue relating to a drug product compounded at a pharmacy and distributed outside the State, the [insert State Board of Pharmacy or other appropriate State agency] will share with FDA, as described in the Submission and Disclosure of Information section of this MOU (section III.c.1.a.iv-v),[7] the results of the investigation as permitted by State law.

7. If the [insert State Board of Pharmacy or other appropriate State agency] receives a complaint involving an adverse drug experience or product quality issue relating to a human drug product compounded by a physician and distributed outside the State, the [insert State Board of Pharmacy or other appropriate State agency] will notify the appropriate regulator of physicians within the State. The [insert State Board of Pharmacy or other appropriate State agency] will also notify FDA by submission to an Information Sharing Network or by sending an email to StateMOU@fda.hhs.gov with the information described in the Submission and Disclosure of Information section of this MOU (section III.c.2.a.-c), if available, as soon as possible, but no later than 5 business days, after receiving the complaint.

b. Distribution of Inordinate Amounts of Compounded Human Drug Products Interstate[8]

1. For purposes of this MOU, a pharmacy has distributed an inordinate amount of compounded human drug products interstate if the number of prescription orders for compounded human drug products that the pharmacy distributed interstate during any calendar year is greater than 50 percent of the sum of:

(i) the number of prescription orders for compounded human drug products that the pharmacy sent out of (or caused to be sent out of) the facility in which the drug products were compounded during that same calendar year; plus

(ii) the number of prescription orders for compounded human drug products that were dispensed (e.g., picked up by a patient) at the

[7] The information includes: (i) [Insert State Board of Pharmacy or other appropriate State agency]'s assessment of whether the complaint was substantiated, if available; and (ii) Description and date of any actions the [insert State Board of Pharmacy or other appropriate State agency] has taken to address the complaint.

[8] The distribution of inordinate amounts of compounded human drug products interstate is a threshold for the [insert State Board of Pharmacy or other appropriate State agency] to identify and report certain information to FDA, not a limit on the distribution of compounded human drug products interstate.

facility in which they were compounded during that same calendar year.

Figure 1. Calculating an Inordinate Amount

$$\frac{A}{B} = X, \text{ where:}$$

A = Number of prescription orders for compounded human drug products that the pharmacy distributed interstate during any calendar year

B = The sum of the number of prescription orders for compounded human drug products (i) that the pharmacy sent out of (or caused to be sent out of) the facility in which the drug products were compounded during that same calendar year; plus (ii) the number of prescription orders for compounded human drug products that were dispensed (e.g., picked up by a patient) at the facility in which they were compounded during that same calendar year

If *X* is greater than 0.5, it is an inordinate amount and is a threshold for certain information identification and reporting under the MOU.

2. On an annual basis, the [insert State Board of Pharmacy or other appropriate State agency] will identify, using surveys, reviews of records during inspections, data submitted to an Information Sharing Network, or other mechanisms available to the [insert State Board of Pharmacy or other appropriate State agency], pharmacies that distribute inordinate amounts of compounded human drug products interstate.

3. For pharmacies that have been identified as distributing inordinate amounts of compounded human drug products interstate during any calendar year, the [insert State Board of Pharmacy or other appropriate State agency] will identify, using data submitted to an Information Sharing Network or other available mechanisms, during that same calendar year:
    a. the total number of prescription orders for sterile compounded human drugs distributed interstate;
    b. the names of States in which the pharmacy is licensed;
    c. the names of States into which the pharmacy distributed compounded human drug products; and
    d. whether the State inspected for and found during its most recent inspection that the pharmacy distributed compounded human drug products without valid prescription orders for individually identified patients.

4. The [insert State Board of Pharmacy or other appropriate State agency] will, within 30 business days of identifying a pharmacy that has distributed inordinate amounts of compounded human drug products interstate, notify FDA of such pharmacy, through an Information Sharing Network or by email to StateMOU@fda.hhs.gov, and will include the

information described in the Submission and Disclosure of Information section of this MOU (section III.c.1.b).

5. If the [insert State Board of Pharmacy or other appropriate State agency] becomes aware of a physician who is distributing any amount of compounded human drug products interstate, the [insert State Board of Pharmacy or other appropriate State agency] will notify the appropriate regulator of physicians within the State. The [insert State Board of Pharmacy or other appropriate State agency] will, within 30 business days of identifying a physician who is distributing any amount of compounded human drug products interstate, also notify FDA by submission to an Information Sharing Network or by email to StateMOU@fda.hhs.gov.

c. Submission and Disclosure of Information
    1. When submitting information using StateMOU@fda.hhs.gov regarding complaints relating to human drug products compounded by a pharmacy and distributed outside the State, or regarding distribution of inordinate amounts of human drug products compounded by a pharmacy interstate, the following minimum information will be included. Note, this information can be submitted to an Information Sharing Network for sharing with FDA.

        a. Complaints:

            i. Name and contact information of the complainant, if available;

            ii. Name and address of the pharmacy that is the subject of the complaint;

            iii. Description of the complaint, including a description of any compounded human drug product that is the subject of the complaint;

            iv. [Insert State Board of Pharmacy or other appropriate State agency]'s assessment of whether the complaint was substantiated, if available; and

            v. Description and date of any actions the [insert State Board of Pharmacy or other appropriate State agency] has taken to address the complaint.

        b. Inordinate Amounts:

i. Name and address of the pharmacy that distributed inordinate amounts of compounded human drug products interstate;

ii. The number of prescription orders for compounded human drug products that the pharmacy sent out of (or caused to be sent out of) the facility in which the drug products were compounded during that same calendar year;

iii. The number of prescription orders for compounded human drug products that were dispensed (e.g., picked up by a patient) at the facility in which they were compounded during that same calendar year;

iv. The total number of prescription orders for compounded human drug products distributed interstate during that same calendar year;

v. The total number of prescription orders for sterile compounded human drug products distributed interstate during that same calendar year;

vi. The names of States in which the pharmacy is licensed and the names of States into which the pharmacy distributed compounded human drug products during that same calendar year; and

vii. Whether the [insert State Board of Pharmacy or other appropriate State agency] inspected for and found during its most recent inspection that the pharmacy distributed compounded human drug products without valid prescription orders for individually identified patients during that same calendar year.

2. When submitting information using StateMOU@fda.hhs.gov regarding complaints relating to human drug products compounded by a physician, or regarding distribution of any amount of human drug products compounded by a physician interstate, the following minimum information will be included, if available. Note, this information can be submitted to an Information Sharing Network for sharing with FDA.

   a. Name and contact information of the complainant or notifier;

   b. Name and address of the physician that is the subject of the complaint or notification; and

c. Description of the complaint or notification, including a description of any compounded human drug product that is the subject of the complaint or notification.

3. The parties to this MOU will share information consistent with applicable statutes and regulations. The parties recognize that a separate agreement under 21 CFR 20.88 may be necessary before FDA can share information that is protected from public disclosure. Such an agreement will govern FDA's sharing of the following types of information:

- Confidential commercial information, such as information that would be protected from public disclosure under Exemption 4 of the Freedom of Information Act (FOIA) (5 U.S.C. 552(b)(4));

- Personal privacy information, such as information that would be protected from public disclosure under Exemption 6 or 7(C) of the FOIA (5 U.S.C. 552(b)(6) and(7)(C)); or

- Information that is otherwise protected from public disclosure by Federal statutes and their implementing regulations (e.g., the Trade Secrets Act (18 U.S.C. 1905), the Privacy Act (5 U.S.C. 552a), other FOIA exemptions not mentioned above (5 U.S.C. 552(b)), the Health Insurance Portability and Accountability Act (Public Law 104-191), and FDA's regulations in parts 20 and 21 (21 CFR parts 20 and 21)).

FDA agrees that information provided to FDA by the [insert State Board of Pharmacy or other appropriate State agency] will only be disclosed consistent with applicable Federal law and regulations governing the disclosure of such information, including the FOIA (5 U.S.C. 552(b)), the FD&C Act (21 U.S.C. 301 et seq.), 21 U.S.C. 331(j), 21 U.S.C. 360j(c), the Trade Secrets Act (18 U.S.C. 1905), FDA's regulations in 21 CFR parts 20 and 21, and other pertinent laws and regulations.

IV. ENFORCEMENT AUTHORITIES AND LEGAL STATUS OF AGREEMENT

The parties to this MOU recognize that FDA and the [insert State Board of Pharmacy or other appropriate State agency] retain the statutory and regulatory authorities provided by the FD&C Act, other Federal statutes and attendant regulations, and State statutes and regulations. The parties also recognize that this agreement does not restrict FDA or any other Federal agency from taking

enforcement action, when appropriate, to ensure compliance with Federal statutes, including the FD&C Act and attendant regulations, or prevent the [insert State Board of Pharmacy or other appropriate State agency] from taking enforcement action, as appropriate, to ensure compliance with applicable State statutes and regulations. This MOU does not create or confer any rights for or on any person. By signing this MOU, the [insert State Board of Pharmacy or other appropriate State agency] affirms that it now possesses and will maintain, at the discretion of the State legislature, the legal authority (under State statutes and/or regulations) and the resources necessary to effectively carry out all aspects of this MOU. If State law changes such that the [insert State Board of Pharmacy or other appropriate State agency] no longer has the legal authority or resources necessary to effectively carry out all aspects of this MOU, the [insert State Board of Pharmacy or other appropriate State agency] will notify FDA within 60 calendar days of the change in legal authority.

V. NAME AND ADDRESS OF PARTICIPATING AGENCIES

U.S. Food and Drug Administration
Center for Drug Evaluation and Research
Office of Compliance
Office of Unapproved Drugs and Labeling Compliance
10903 New Hampshire Avenue
Bldg. 51, Suite 5100
Silver Spring, MD 20993-0002
Telephone: (301) 796-3110
Email: StateMOU@fda.hhs.gov

[Insert State Board of Pharmacy or other appropriate State agency and its contact information]

Upon signing the MOU, each party must designate one or more liaisons to act as points of contact. Each party may designate new liaisons at any time by notifying the other party's liaison(s) in writing. If, at any time, an individual designated as a liaison under this agreement becomes unavailable to fulfill those functions, the parties will name a new liaison within 2 weeks and notify the other party's liaison(s).

VI. PERIOD OF AGREEMENT

a. When accepted by both parties, this MOU will be effective from the date of the last signature and will continue until terminated by either party. It may be terminated in writing by either party, upon a 60 calendar day notice of termination. Notice of termination will be sent to the address listed in section V of this MOU.

b. If the [State Board of Pharmacy or other appropriate State agency] does not adhere to the provisions of this MOU, including conducting an investigation of complaints related to compounded human drug products distributed outside the State, the MOU may be terminated upon a 60 calendar day notice of termination.

In case of termination, FDA will post a notice of the termination on its Web site and the [insert State Board of Pharmacy or other appropriate State agency] will notify all pharmacies that compound drug products in the State and notify the State authority that licenses or regulates physicians of the termination and advise them that as of 60 calendar days from the date of the posting of the termination notice, compounded human drug products may be distributed (or caused to be distributed) out of the State only "in quantities that do not exceed 5 percent of the total prescription orders dispensed or distributed" by the licensed pharmacy or physician (section 503A(b)(3)(B)(ii) of the FD&C Act).

VII. APPROVALS

APPROVED AND ACCEPTED FOR THE U.S. FOOD AND DRUG ADMINISTRATION	APPROVED AND ACCEPTED FOR [insert State Board of Pharmacy or other appropriate State agency]
By (Type Name)	By (Type Name)
Title	Title
Date	Date

Appendix A. Definition of Terms for the Purposes of this MOU

- **Adverse Drug Experience**: Any adverse event associated with the use of a drug in humans, whether or not considered drug related, including the following: an adverse event occurring in the course of the use of a drug product in professional practice; an adverse event occurring from drug overdose, whether accidental or intentional; an adverse event occurring from drug abuse; an adverse event occurring from drug withdrawal; and any failure of expected pharmacological action (21 CFR 310.305(b)).

- **Distribution of compounded human drug products interstate**: Means that a pharmacy or physician has sent (or caused to be sent) a compounded drug product out of the State in which the drug was compounded.

- **Information Sharing Network:** An information sharing network designated by FDA for purposes of this MOU to collect, assess, and allow review and sharing of information pursuant to this MOU.

- **Inordinate Amounts**: A pharmacy has distributed an inordinate amount of compounded human drug products interstate if the number of prescription orders for compounded human drug products that the pharmacy distributed interstate during any calendar year is greater than 50 percent of the sum of: (i) the number of prescription orders for compounded human drug products that the pharmacy sent out of (or caused to be sent out of) the facility in which the drug products were compounded during that same calendar year; plus (ii) the number of prescription orders for compounded human drug products that were dispensed (e.g., picked up by a patient) at the facility in which they were compounded during that same calendar year.[9]

- **Product Quality Issue**: Information concerning (1) any incident that causes the drug product or its labeling to be mistaken for, or applied to, another article; or (2) any bacteriological contamination; any significant chemical, physical, or other change or deterioration in the distributed drug product; or any failure of one or more distributed batches of the drug product to meet the applicable specifications (21 CFR 314.81(b)(1)). Contamination in general, including but not limited to mold, fungal, bacterial, or particulate contamination, is a product quality issue.

- **Serious Adverse Drug Experience**: Any adverse drug experience occurring at any dose that results in any of the following outcomes: death, a life-threatening adverse drug experience, inpatient hospitalization or prolongation of existing hospitalization, a persistent or significant disability/incapacity, or a congenital

[9] The definition of *inordinate amounts* in this MOU is separate and distinct from and should not be used in relation to the term *inordinate amounts* as it is used in section 503A(b)(1)(D) of the FD&C Act (pertaining to compounding a drug product that is essentially a copy of a commercially available drug product). The interpretation of this term in each instance necessarily is based on the particular context of the distinct provisions within 503A in which the term appears.

anomaly/birth defect. Important medical events that may not result in death, be life-threatening, or require hospitalization may be considered a serious adverse drug experience when, based upon appropriate medical judgment, they may jeopardize the patient or subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition. Examples of such medical events include allergic bronchospasm requiring intensive treatment in an emergency room or at home, blood dyscrasias or convulsions that do not result in inpatient hospitalization, or the development of drug dependency or drug abuse (21 CFR 310.305(b)).

- **Serious Product Quality Issue**: Any product quality issue that may have the potential to cause a serious adverse drug experience (e.g., possible contamination, superpotent product).

TEXAS STATE BOARD OF PHARMACY

June 15, 2020

The Honorable Russell Vought
Director
Office of Management and Budget
725 17th Street NW
Washington, DC 20503

Submitted via: https://www.regulations.gov/comment?D=FDA-2018-N-3065-0046

RE: Comments on Memorandum of Understanding Addressing Certain Distributions of Compounded Drug Products Between the States and the Food and Drug Administration; Revised Draft; Availability (OMB Control Number 0920-0800; Docket ID: FDA-2018-N-3065)

Dear Director Vought:

This letter is to express concerns with the information collection that has recently been submitted to Office of Management and Budget (OMB) by the Food and Drug Administration (FDA) for review under the Paperwork Reduction Act dealing with the "Memorandum of Understanding Addressing Certain Distributions of Compounded Human Drug Products Between [insert State of Pharmacy or Other Appropriate State Agency] and the U.S. Food and Drug Administration" (MOU). The MOU will require substantial inspection, data tracking, reporting and recordkeeping requirements on boards of pharmacy and other agencies in states that sign the MOU, so the FDA estimates of the burden for those requirements are critical.

The Texas State Board of Pharmacy has not been formally surveyed or otherwise directly contacted regarding FDA's collection of information for the MOU. Instead, the notice of the collection of information filed with OMB suggests that FDA has based their estimates of both how many states will sign the MOU and what the burden on those states will be on a handful of comments from state boards. From these comments, FDA estimates the average numbers for how many adverse event reports states will receive and how many pharmacies will trigger the 50% threshold on out-of-state distributing and dispensing drugs, which then requires tracking, reporting and recordkeeping. An accurate information collection by FDA would have involved actually surveying states in writing, and as result, the lack of accurate information may have resulted in a serious underestimation of the burden the MOU will have for boards. The estimate of the number of states that will sign the MOU could also be inflated. The burden on larger states that sign the MOU, like Texas, will undoubtedly be several times greater than the averages in FDA's estimates.

FDA disagrees with comments they received that the MOU amounts to an unfunded mandate because it is "voluntary". However, FDA's defines the term "distribution" in the MOU to include patient specific dispensing. As a result, if a state does not sign, the economic impact on pharmacies and the healthcare impact on their out-of-state patients would be considerable. It would be critical that FDA conduct a comprehensive collection of information on the MOU so that OMB, as well state boards of pharmacy, state legislatures, pharmacy stakeholders and the public can have a more complete picture of what state resources will be necessary to meet the MOU's requirements.

We also have specific concerns regarding the content of two sections of the MOU.

1. Section III.a.5 provides:

> As soon as possible, but no later than 5 business days after receiving a complaint involving a serious adverse drug experience or serious product quality issue relating to a drug product compounded at a pharmacy and distributed outside the State, the [insert State Board of Pharmacy or other appropriate State agency] will, by submission to an Information Sharing Network5 or by email to StateMOU@fda.hhs.gov, provide FDA with the information described in the Submission and Disclosure of Information section of this MOU (section III.c.1.a.i-iii).

This provision should be changed to require the submission as soon as possible, but no later than 5 business days after *discovering* that a complaint involves a serious adverse drug experience or serious product quality issue. Complaints are often submitted without complete information regarding the circumstances, including whether the incident involved a serious adverse drug experience or serious product quality issue and whether drug product compounded at a pharmacy and distributed outside the State. As written this section would potentially require the agency to report a complaint before identifying that the complaint met the requirements for reporting.

2. Section III.b.3.d provides:

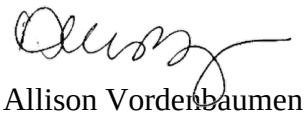
> 3. For pharmacies that have been identified as distributing inordinate amounts of compounded human drug products interstate during any calendar year, the [insert State Board of Pharmacy or other appropriate State agency] will identify, using data submitted to an Information Sharing Network or other available mechanisms, during that same calendar year:
> . . .
> d. whether the State inspected for and found during its most recent inspection that the pharmacy distributed compounded human drug products without valid prescription orders for individually identified patients.

This section is confusing and in conflict with the stated purpose of the MOU. If a pharmacy distributes compounded human drug products without valid prescription orders for individually identified patients, then it would be compounding drugs as a 503B outsourcing

facility and would fall outside the scope of the MOU which states that it does not apply to 503B facilities. Further, the Texas State Board of Pharmacy does not regulate outsourcing facilities.

I appreciate the opportunity to provide comments. Thank you for your consideration of our input. Please do not hesitate to contact me with any questions or concerns.

Sincerely,



Allison Vordenbaumen Benz, R.Ph., M.S
Executive Director/Secretary

NABP
National Association of Boards of Pharmacy

Preparing for FDA's Compounding MOU

Melissa Madigan, PharmD, JD
National Association of Boards of Pharmacy
Associate Executive Director, Professional Affairs

NABP
National Association of Boards of Pharmacy

FDA's Compounding MOU Raises Questions Among Boards of Pharmacy

The impending implementation of the Food and Drug Administration (FDA) "Memorandum of Understanding Addressing Certain Distributions of Compounded Human Drug Products" (MOU) has introduced many questions among the state boards of pharmacy.

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Questions Include:

- When will the MOU be finalized?
- What obligations will it place on the boards of pharmacy?
- How will it impact state oversight of 503A pharmacies?
- What information will be required to collect and share?
- What IT and personnel resources will be needed?
- What mechanism will be used to collect, manage, and share information?
- When does a board need to share complaints regarding compounders with the FDA?
- Do “prescription orders” include new and refill prescription orders?
- What will FDA do with submitted information?
- What happens if a state doesn’t comply with the MOU?
- Regarding submission of complaint information, should the board include PHI, such as patient names or other identifiers? Or should PHI be redacted?

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What Information Must Boards of Pharmacy Flag for FDA?

- Certain compounding pharmacy data
- Certain complaints about compounding pharmacies
- Certain complaints about compounding physicians
- Certain information about compounding physicians distributing interstate

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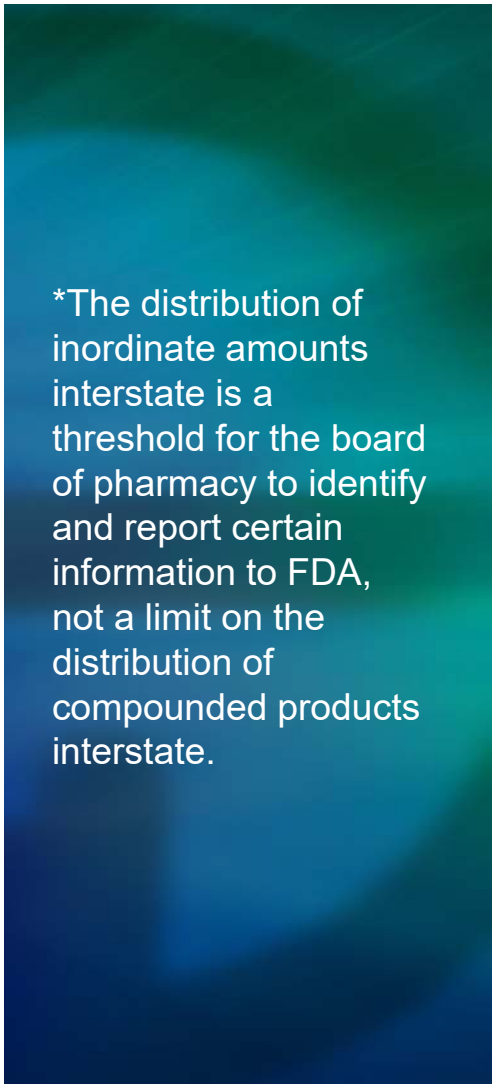
What Information Must Boards of Pharmacy Flag for FDA?

Per the MOU, boards must identify for FDA:

- Pharmacies that are compounding human drug products and distributing inordinate amounts interstate*
- Complaints of serious adverse experiences or quality issues relating to human drug products compounded by pharmacies and distributed interstate
- Complaints of adverse experiences or quality issues relating to human drug products compounded by a physician and distributed interstate
- Information relating to the distribution interstate of any amount of compounded human drug products by physicians



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Regarding “Inordinate Amounts:”

- Boards will determine if a pharmacy is compounding inordinate amounts using either:
  - Surveys, or
  - reviews of records during inspections, or
  - information-sharing network (NABP’s system), or
  - other available mechanisms
- The MOU does not require the board to input compounding pharmacy data into the information-sharing network.
- The MOU allows the board to meet its obligation to determine compounding of inordinate amounts solely through use of the information-sharing network.

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NABP Develops System for Collecting and Sharing Information Specified in the MOU

- The information-sharing network is being developed using a grant provided by FDA to NABP
  - Grant is for a pilot project to build a network and evaluate its accuracy and usefulness
- FDA recognized there is no centralized system to collect and share data from compounding pharmacies distributing interstate, and thus the grant was established
- FDA is eager to partner with NABP and boards to protect patients from high-risk compounders
- FDA agrees the network will be a key to assisting boards in their efforts to comply with the MOU, understanding the lack of board resources

NABP
National Association of Boards of Pharmacy

How is NABP Building the New Information Sharing System?

- NABP is adapting its existing NABP e-Profile Connect data management system to meet the needs of the new information-sharing network
  - to enable the collection, management, and sharing of information pertaining to compounders
- e-Profile Connect provides state boards of pharmacy with information on each individual pharmacist, technician, student/intern, and facility in the system

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System Will Provide New Capabilities for Boards of Pharmacy

- Expands current e-Profile Connect system
- Adds data fields outlined in the MOU to the pharmacy facility profiles found in the e-Profile Connect system
- Allows boards and pharmacies to enter data
- Boards will be able to review and annotate information provided by licensees, and upload documents, including complaints and inspection forms

NABP
National Association of Boards of Pharmacy

Implementation Begins with Pilot Project

- Development of the new information-sharing network began in June 2020 as part of the three-year pilot project
- Implementation of the network is expected to begin in early 2021 with the collection of information from compounding pharmacies
- Boards of pharmacy will have access to this information and the ability to supplement it soon after pharmacies can begin inputting data
- At the conclusion of the pilot project, NABP will evaluate the usability of the network and the accuracy of the information collected during the pilot and present a final analysis to FDA

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System Will Identify Certain Data for FDA

- The system will notify boards about pharmacies whose submitted data show that they are distributing inordinate amounts of compounded human drugs interstate
- The system will require boards of pharmacy to approve the submission of such data to FDA prior to it being transmitted

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What Information Will Be Collected From Pharmacies?

Regarding the distribution or dispensing of compounded human drug products, the system will collect the following information from the pharmacy:

- Name and address of state-licensed entity
- Whether the pharmacy participates in the following activities during an identified calendar year:
  - Human drug compounding – sterile
  - Human drug compounding – nonsterile
  - Patient-specific compounding
  - Non-patient-specific compounding

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If a Pharmacy Is Compounding Sterile or Nonsterile Human Drug Products, the Following Information Will Also Be Collected or Calculated:

- Number of prescription orders for compounded drugs the pharmacy sent out
- Number of prescription orders for compounded drugs dispensed at the facility
- Total number of prescription orders for compounded drugs sent out or dispensed at the facility*
- Total number of prescription orders for compounded drugs distributed interstate
- Percentage of compounded drugs distributed interstate*

*Calculated by the system

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Also to Be Collected:

- Number of prescription orders for sterile compounded drugs distributed interstate
- Names of states in which pharmacy is licensed
- Names of states into which pharmacy distributed compounded drugs during the year
- Whether compounded drugs are distributed without patient-specific prescriptions

If the board has the compounding pharmacy data referenced here, the board will be able enter it into the facility's e-profile.

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Notifying FDA of Inordinate Amounts

Within 30 business days of identifying a pharmacy that has distributed inordinate amounts of compounded human drugs interstate during the identified calendar year, and upon approval by the board, the system will provide FDA with the following information about such pharmacies:

1. Name and address of the pharmacy
2. The number of prescription orders for compounded human drugs that the pharmacy sent out of (or caused to be sent out of) the facility in which the drugs were compounded
3. The number of prescription orders for compounded human drugs that were dispensed (e.g. picked up by the patient) at the facility in which they were compounded

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Notifying FDA of Inordinate Amounts

4. The total number of prescription orders for compounded human drugs distributed interstate
5. The total number of prescription orders for sterile compounded human drugs distributed interstate
6. The names of the states in which the pharmacy is licensed
7. The names of the states in which the pharmacy distributed compounded human drugs
8. Whether the board inspected for and found during its most recent inspection that the pharmacy distributed compounded human drugs without valid prescription orders for individually identified patients

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Notifying FDA of Pharmacy Complaints

Regarding complaints involving a serious adverse drug experience or serious product quality issue related to human drug products compounded by a pharmacy and distributed outside the state, the board will enter into the system:

1. Name and contact information of the complainant, if available
2. Name and address of pharmacy that is the subject of complaint
3. Description of complaint, including description of any compounded human drug product that is the subject of complaint
4. The board's assessment of whether the complaint was substantiated, if available
5. Description of any actions the board has taken to address the complaint

The board will also be able to upload a copy of the complaint or other relevant documents.

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Notifying FDA of Pharmacy Complaints

Transmission of complaint information from system to FDA:

- As soon as possible after, but no later than five business days after receiving the complaint, and upon approval by the board, the system will provide FDA with the information found in items 1 – 3.
- After the board concludes its investigation of the compliant, and upon approval by the board, the system will provide FDA with the information found in items 4 – 5.

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Notifying FDA of Complaints and Notifications about Physicians

Regarding complaints involving an adverse drug experience or product quality issue related to human drug products compounded by a physician, or regarding the distribution of any amount of human drug products compounded by a physician and distributed outside a state, the board will enter into the system:

1. Name and contact information of the complainant or notifier
2. Name and address of the physician who is the subject of the complaint or notification
3. A description of the complaint or notification, including a description of any compounded human drug product that is the subject of the complaint or notification.

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Notifying FDA of Complaints and Notifications about Physicians

Transmission of Physician Complaint Information from system to FDA:

- Regarding complaints against physicians, as soon as possible but no later than five business days after receiving the complaint, and upon approval by the board, the system will transmit such complaint to FDA. In addition, the board must notify the state regulator of physicians.

Transmission of Physician Notification Information from system to FDA:

- Regarding the distribution of any amount of compounded products interstate by a physician, within 30 business days of identification of such physician, and upon approval by the board, the system will transmit this information to FDA. In addition, the board must notify the state regulator of physicians.

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Collection of Data From Pharmacies Will Be Through Two Pathways

1. Requesting compounding data through any application for one of our pharmacy accreditation programs *except* for the DMEPOS program, or through the VPP inspection application. The pharmacy will pay the regular accreditation or inspection application fee.
2. The data fields will be available through the pharmacy's e-profile. The pharmacy will set up an e-profile or access its already-established e-profile, then insert the data. There is no charge for this.

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How will NABP Encourage Pharmacies to Volunteer Requested Information?

- All pharmacies seeking accreditation will voluntarily submit the requested information – regardless of whether their primary intent is to participate in the pilot project
- Compounding pharmacies can enter the requested information outside of the accreditation application process
- All pharmacies submitting the requested data will have the opportunity to receive a VPP inspection at no cost to them.

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How Will the System Meet the Goal of Improving Compounding Pharmacy Oversight?

- Enable the collection, management, and sharing of information regarding compounding pharmacies in the US
- Provide boards of pharmacy with a tool to report compounding pharmacy information to FDA, giving access to data that will inform oversight determinations
- Enable boards of pharmacy to better prioritize their resources to address compounding pharmacies that pose the highest risk to patients
- Foster better, more targeted oversight of compounding pharmacies

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Project Provides Transparency to Support Data-Driven Policy Decisions

- Boards of pharmacy and FDA will gain a better understanding of the interstate distribution of compounded drugs, including significant compliance issues
- Boards of pharmacy and FDA will be better positioned to advance public health protections associated with compounded drugs
- Boards of pharmacy will gain an ongoing means of reporting information relating to compounding pharmacies to FDA
- FDA will gain improved visibility to determine whether additional federal oversight is warranted

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Feedback from Boards Has Been Positive

- Vast majority of boards are in the process of determining whether to sign the MOU.
- Several boards have said they will surely sign the MOU.
- Some boards have said they do currently require or are considering requiring pharmacies to report data to the system.
- Very few have said they will not sign the MOU.
- NABP is in conversations with several boards about sharing compounding pharmacy data they already collect.

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Informational Resources

NABP's new website has a page dedicated to this project

- Background and details on the project
- Link to MOU
- FAQs
- Slide deck

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Thank You!

Alliance for Pharmacy Compounding

November 9, 2020

Allison Vordenbaumen Benz
Executive Director / Secretary
Texas State Board of Pharmacy
333 Guadalupe, Ste #3-500
Austin, TX 78701

RE: FDA's Final MOU on Interstate Distributions of Compounded Drug Products

Dear Allison:

As you may be aware, on October 26, 2020, the Office of Management and Budget (OMB) cleared the Food and Drug Administration's (FDA's) Memorandum of Understanding (MOU) on interstate distributions of compounded drug products under the Paperwork Reduction Act – and on the following day FDA posted the final MOU in the Federal Register and made it available for states to sign. The Notice of Availability can be found here (*hyperlink)* and the final MOU can be found here (*hyperlink)*. The notice indicates that states will have one year to sign the MOU before FDA begins enforcing a statutory five percent cap on interstate distributions – defined by FDA to include traditional dispensing – from pharmacies in states that do not sign the MOU.

When the final MOU was sent to OMB in May of this year, the Alliance for Pharmacy Compounding (APC) joined other stakeholders, including major national pharmacy organizations (National Community Pharmacists Association, American Pharmacists Association, National Alliance of State Pharmacy Associations), Members of Congress, multiple state boards of pharmacy, and many individual pharmacists and pharmacy owners to express serious concerns that FDA had not met the requirements of the Paperwork Reduction Act to do a collection of information on the administrative and financial burdens the MOU's unfunded mandates would place on states. As many stakeholders pointed out, the collection of information in this particular case was critically important because the burden and cost of the unfunded mandates on state boards of pharmacy relate directly to how many states will sign the MOU.

Pharmacies in states that cannot sign – due to restrictions in state law, or because they don't have the financial resources to meet the MOU's mandates, or they choose not to sign because of the requirements it will place on state agencies and pharmacies in their state – will be capped at distributing no more than five percent of their compounded drug products interstate. Because FDA has redefined in the MOU the key term of distribution to include the patient-specific dispensing of compounded drugs, pharmacies in states that don't sign the MOU will be capped at "distributing" or "dispensing" no more than five percent of their compounded drugs out of state. This has the potential to create an enormous patient access problem for the millions of Americans who rely on medications compounded at out-of-state pharmacies. This is why a true collection of information by FDA about the impact of the MOU on each state and the status of legal authority, financial capability and overall likelihood of each state to sign the final MOU was so important.

Unfortunately, instead of surveying each state about these important questions, FDA simply asked for comments from states and from the few they got, gleaned national state averages about the burden the FDA estimates will be placed on state agencies. Amazingly, although the information submitted to OMB from FDA estimates a total annual time burden (in hours) of the MOU on states at 7,789, *it also asserts*

$0 in annual cost burden (in dollars) of the MOU on the states. FDA's estimate that 45states will sign the final MOU is not supported by any survey of the states or empirical evidence and is inconsistent with NABP's estimate and comments both FDA and OMB have received directly from state boards of pharmacy. For these reasons, APC and many other stakeholders asked OMB to reject the MOU under the Paperwork Reduction Act and send it back to the FDA for a true collection of information about the burden of the MOU on state agencies and whether states intended to sign the now finalized MOU. Unfortunately, OMB chose to ignore all of this stakeholder input and clear the MOU without change, triggering the 365-day clock for states to decide whether or not to sign the MOU.

It is particularly troubling that FDA would finalize this MOU without going through the notice and comment rulemaking process under the Administrative Procedures Act, as clearly called for in the statutory language of section 503A of the Food, Drug and Cosmetic Act (FDCA) that establishes the MOU requirement. This is unfortunately part of a larger pattern of FDA implementing and enforcing the compounding provisions of the FDCA, as amended by the Drug Quality and Security Act (DQSA) of 2013, through informal, non-binding guidance documents rather than going through the more rigorous rulemaking process that is intended to provide more stakeholder input and greater transparency and accountability for federal agencies implementing the laws passed by Congress.

APC believes that had this MOU gone through the rulemaking process as clearly called for in the statute, a final MOU would have been developed that had broad stakeholder support and that all or nearly all 50 states would sign. Instead, in defiance of Congress, FDA short-circuited the process to finalize a substantively flawed MOU that redefines key statutory terms in an attempt to give the agency authority over the patient-specific dispensing of compounded drugs, which as you know is traditionally regulated under state law. We are concerned that a full collection of information would show that many more than FDA's estimate of five states cannot or will not sign this MOU – and that an entirely avoidable access crises is brewing for the patients who rely on pharmacies in those states for their compounded medications. Indeed, a federal lawsuit has already been filed by a coalition of several compounding pharmacies, seeking declaratory relief that the MOU should be vacated because it did not go through rulemaking as called for in the statute and because it clearly exceeds the statutory authority granted to FDA by Congress.

States that sign the MOU will be required to finance the additional staffing needed to gather intrastate and interstate dispensing and distribution data from all compounding pharmacies in their state and evaluate that data to determine which pharmacies trigger the MOU's reporting requirements. States that sign the MOU will further be required to investigate adverse event reports, report data to the FDA, and maintain records. Pharmacies in states that are unable or unwilling to sign the MOU are statutorily prohibited from "distributing" more than five percent of their compounded drugs interstate. In the MOU the FDA directs states to use "surveys, reviews of records during inspections, data submitted to an Information Sharing Network, or other mechanisms available" to determine which pharmacies in their state have distributed more than 50 percent of their compounded drugs out of state.

While the outcome of this lawsuit or other potential litigation related to the MOU is uncertain, APC remains committed to working with pharmacy stakeholders to provide much-needed public information about the impact the MOU will have on states that sign and the pharmacies in those states, as well as the impact it will have on the pharmacies that don't sign the MOU and the out-of-state patients those pharmacies serve. We are committed to continuing to strive for a workable final MOU that gives FDA the data they need to track inordinate interstate shipments of compounded drugs without unduly burdening states or inappropriately capping patient-specific dispensing. We believe more public

information about the current MOU is needed to accomplish this goal. **To that end, we respectfully ask that you or your Board's legal counsel take a few minutes to complete our brief survey, either online at www.a4pc.org/stateMOUsurvey or enclosed here (to be returned to us by fax or email).**

Thank you in advance for your participation in this important collection of information on the MOU that has unfortunately become necessary due to FDA's failure to complete one pursuant to the Paperwork Reduction Act. Should you have any questions or concerns, please do not hesitate to contact me directly at scott@a4pc.org or 404-844-8607.

Sincerely,

Scott Brunner, CAE
Chief Executive Officer
scott@a4pc.org

ENCLOSED: Questionnaire

Alliance for Pharmacy Compounding

STATE BOARD OF PHARMACY QUESTIONNAIRE

ON FDA'S MOU ON INTERSTATE DISTRIBUTIONS OF COMPOUNDED MEDICATIONS

Please complete the questionnaire below no later than November 30, 2020 if possible and fax it to the Alliance for Pharmacy Compounding at (281) 495-0602 or scan and email it to info@a4pc.org. Or if you prefer, you may complete the questionnaire online at www.a4pc.org/stateMOUsurvey. Thank you.

1. STATE NAME:
2. STATE BOARD OR AGENCY NAME:
3. YOUR NAME:
4. YOUR TITLE:
5. YOUR EMAIL ADDRESS:
6. Under your state's law, does the state board of pharmacy have the legal authority to sign the MOU with FDA? If not, is there another agency in your state that does? If so which one?

7. If the answer to question #1 is no, what action would be necessary to give your Board or another state agency the legal authority to sign the MOU? (e.g. a change to state law, a proposed regulation, a change to Board rules)

8. 3. How many pharmacies in your state do you estimate are currently distributing and dispensing more than 50 percent of their compounded drugs out-of-state?

9. How many annual manpower hours do you estimate it would take your Board to collect and evaluate data on intrastate and interstate shipments of compounded drugs from pharmacies licensed in your state?

10. How many additional annual manpower hours do you estimate would be required for your Board to meet the MOU's requirements to investigate adverse events (including additional inspectors) related to compounded drugs shipped interstate from pharmacies in your state?

11. How many additional annual manpower hours do you estimate would be required for your Board to meet the MOU's reporting and recordkeeping requirements?

12. Do you anticipate that the MOU would require your Board to hire additional full or part-time employees? If so, how many?

13. Roughly, what do you estimate the overall annual financial burden (in dollars) to your state would be to comply with the mandates associated with the MOU?

14. What amount, if any, has your state budgeted for fiscal year 2021 to meet the mandates of the MOU?

15. Does your state intend to sign the final MOU?

Return completed questionnaire by fax to the Alliance for Pharmacy Compounding at (281) 495-0602 *or scan and email it to info@a4pc.org no later than NOVEMBER 30, 2020 if possible.*

If you have questions, please contact APC's David Pore at dpore@hslawmail.com.