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Business, Consumer Services and Housing Agency
Department of Consumer Affairs
Gavin Newsom, Governor

Enforcement and Compounding Committee Report

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The Board will review a summary of the committee's work at its February 18, 2021 and April 22, 2021, meetings as well as updates for discussion and action as necessary

a. Summary and Discussion on the Informational Meeting on "White Bagging"

On February 18, 2021, the Enforcement and Compounding Committee hosted an informational meeting on "white bagging" which refers to the distribution of patient-specific medication from a pharmacy, typically a specialty pharmacy, to the physician's office, hospital or clinic for administration. It is often used in oncology practices to obtain costly injectable and infusible medications that are distributed by specialty pharmacies and may not be available in all non-specialty pharmacies.

The committee publicized this informational meeting and reached out to identified stakeholders to participate in the informational meeting. The committee heard from various stakeholders on the practice of "white bagging" with the goal of receiving numerous perspectives on this practice to ensure the education on the matter was comprehensive. An overview of the informational meeting will be provided during the committee report.

b. Summary of Presentation on the National Association of Boards of Pharmacy, Compounding Data Sharing Project

Relevant law
Federal law establishes provisions for pharmacy compounding in Section 503A of the FD&C Act. Further, as provided in this section, the FD&C Act directs the FDA to develop a standard Memorandum of Understanding (MOU), in consultation with the National Association of Boards of Pharmacy.

Background
In October 2020, the FDA finalized its draft MOU, that establishes an agreement between the respective state authority and the FDA regarding the distribution of inordinate amounts of

compounded human drug products interstate and the appropriate investigation by respective state authority of complaints of such products.

The MOU establishes various conditions that respective state authorities must adhere to as a condition of the agreement including:

1. **Investigation of Complaints Relating to Compounded Human Drug Products Distributed Outside the State**
   The state authority will investigate complaints of adverse drug experiences and product quality issues related to human drug products compounded at a pharmacy in its jurisdiction that is distributed outside of the state. As part of the investigation the state authority must assess whether there is a public health risk association with the compounding product. Further, the state agency must maintain records for at least three years, compels the state authority to report complaints involving serious adverse drug experience or serious product quality issues within five business days of receipt, and mandates reporting of investigation outcomes to the FDA. The state authority is also required to notify the appropriate regulatory authority of physicians in the jurisdiction, if the complaint involves product compounded by a physician and distributed interstate.
2. **Distribution of Inordinate Amounts of Compounded Human Drug Products Interstate**
   Defines inordinate amount as the number of prescription orders that a pharmacy distributed interstate during any calendar year that is greater than 50 percent of the number of prescription orders sent out of state versus the total number of prescription orders dispensed. Requires the state authority to identify such compounding pharmacies and notify the FDA within 30 days of such a determination and requires the state authority to notify the appropriate regulator of physicians, if the state authority is aware of a physician distributing an inordinate amount.
3. **Submission and Disclosure Information**
   Prescribes the minimum information that must be provided, specifies that the information can be provided via the Information Sharing Network, and establishes authority for sharing such information under a separate agreement as provided for in 21 CFR 20.88.

During the meeting members will receive a presentation by NABP and the FDA on the Compounding Pharmacy Information-Sharing Project, which is intended to help facilitate some of the provisions of the MOU.

Attachment 1 includes a copy of the presentation slides information and summary information provided by the NABP.

c. Discussion and Consideration of FDA's Final MOU on Interstate Distribution of Compounded Drug Products

Background

During its prior discussion, the Committee received significant public comment requesting the Board enter into the MOU. Further, the Committee requested that staff determine if an extension could be secured to allow for implementation of necessary provisions should the Board determine signing the MOU is appropriate. Staff is awaiting a response on this issue and will provide an update should one be available during the meeting.

Review of summary implementation information provided by NABP reveals that states are in various stages of consideration of the issue. To date, only one state has signed the MOU and several states have declined. Several states have concluded they are unable to participate in the MOU because of legal or technical reasons, while some are considering regulations. Seven states are in the process of entering the MOU, pending additional action.

Staff and counsel recently attended a listening session with FDA representatives. As part of the session, concern was raised about the implementation timeline and other challenges with satisfying the requirements of the MOU, including the need for statutory changes in California before it could enter into the MOU if deemed appropriate. Staff have requested a follow up discussion with the FDA that has not been scheduled yet.

<u>For Discussion and Consideration</u>
During the meeting members will have the opportunity to discuss the MOU. It is recommended that the committee consider larger questions as part of its discussion including:

1. Does the Board have the authority to enter into the MOU?
2. What are the potential benefits and negative impacts to California consumers for the Board to enter into this agreement?
3. What are the potential positive and negative impacts to compounding pharmacies and residents outside of California if the Board does not enter into the MOU?

Should the committee agree that entering into the MOU is appropriate, the following implementation issues need to be considered. Such changes will need to be facilitate through statutory changes.

1. Should the Board require as a condition of renewal, that a pharmacy advise the Board that it distributes compounded preparations outside of California?
2. Should the Board establish a requirement for such pharmacies to report sales to the Information Sharing Network as provided for in the MOU?
3. Should the Board establish a requirement for pharmacies to report adverse drug experiences and drug quality issues related to a drug compounded at a pharmacy?
   Note: Staff suggest harmonizing the language of BPC 4127.1(f) for sterile products to include mandatory reporting of all adverse drug experiences and compounded drug quality issues. Further either a statutory change would be required to establish the mandatory reporting for nonsterile products.
4. Should we require pharmacies that engage in interstate compounding to affirm their understanding of the conditions detailed in the MOU that must be fulfilled to engage in interstate compounding?
5. Should the Board establish confidentiality provisions for the information provided to the FDA directly or through the Information Sharing Network.
6. Should the Board develop education materials for pharmacies that distribute compounded product interstate.

Attachment 2 includes a copy of the MOU, questions and answers released by the FDA, a draft statutory proposal that provides an example of statutory changes that could be used facilitate implementation, and written comments received.

d. Discussion and Consideration of Compounding with Components or Other Materials that Could Result in Insanitary Conditions as Established in the FDA Insanitary Conditions at Compounding Facilities Guidance for Industry

Relevant Law

Under section 501(a)(2)(A) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 351(a)(2)(A)), a drug is deemed to be adulterated "if it has been prepared, packed, or held under insanitary conditions whereby it may have been contaminated with filth, or whereby it may have been rendered injurious to health . . ." Drug products prepared, packed, or held under insanitary conditions could become contaminated and cause serious adverse events, including death.

Under sections 503A and 503B of the FD&C Act (21 U.S.C. 353a and 353b), compounded human drug products can qualify for exemptions from specified provisions of the FD&C Act if certain conditions are met. However, neither section provides an exemption from section 501(a)(2)(A) of the FD&C Act. Drugs (including biological products) prepared, packed, or held (hereinafter referred to as "produced") under insanitary conditions are deemed to be adulterated, regardless of whether the drugs qualify for exemptions set forth in sections 503A or 503B of the FD&C Act.

Section 503A of the Food, Drug & Cosmetic Act (FD&C Act), includes certain restrictions on the bulk drug substances that can be used in compounding and directs the FDA to develop a list of bulk substances that can be used in compounding under section 503A.

Under the conditions of the law, one of the conditions that must be met for a compounded drug product to qualify for these exemptions is that a licensed pharmacist compounds the drug product using bulk drug substances that:

1. Comply with the standards of an applicable USP-NF monograph, if a monograph exists, and the USP chapter on pharmacy compounding;
2. If such a monograph does not exist, are drug substances that are components of drugs approved by the Secretary, or,
3. If such a monograph does not exist and the drug substance is not a component of a drug approved by the Secretary, appears on a list developed by the Secretary through regulations issued by the Secretary under subsection (c) of section 503A.

Note: FDA has interpreted "an applicable USP or NF monograph to mean an official USP or NF drug substance monograph. **Accordingly, the FDA does not consider USP monographs for dietary supplements to be "applicable USP or NF monographs within the meaning of section 503A(b)(1)(A(i)(I)".**

Further, Section 503B of the FD&C Act directs the FDA to develop a list of bulk drug substances for which there is a clinical need. Drug products compounded using bulk drug substances on the 503B bulks list quality for certain exemptions from the FD&C Act provided the other conditions in section 503B are met. As provided in federal law, outsourcing facilities are subject to FDA inspections and other conditions that help to mitigate the risks of the drug products they compound. Further, bulk

drug substances used by outsourcing facilities must be accompanied by a valid certificate of analysis and must have been manufactured by an establishment registered with the FDA under section 510 of the FD&C Act. In addition, if an applicable USP or National Formulary drug monograph exists, bulk drug substances must comply with the monograph and will be taken off the bulk substances list.

Background

In November 2020, the FDA finalized and released its guidance document describing examples of insanitary condition that the FDA has observed. As indicated in the document, the guidance specifically addresses drugs (including biological products) produced in settings including pharmacies and outsourcing facilities that compound, mix, dilute or repackage drugs, including biological products.

The FDA notes in its guidance document the following:

> "In addition, to protect the public health, both FDA and state regulatory agencies may take action when compounding facilities produce drugs under insanitary conditions. Based on its inspections, FDA determines whether compounding facilities produce drugs under insanitary conditions in violation of section 501(a)(2)(A) of the FD&C Act, and if so, the Agency may initiate regulatory action. However, compounding facilities that are not registered with FDA as outsourcing facilities are primarily overseen by the states and, as explained above, generally are not routinely inspected by FDA. FDA strongly encourages state regulatory agencies to assess during inspections whether compounding facilities that they oversee engage in poor practices, including those described below. Where insanitary conditions are identified, FDA encourages states to take appropriate action, consistent with state laws and regulations, and to contact FDA."

This issue of compounding a sterile preparation using a bulk ingredient is very complex, requiring pharmacies to understand and adhere to not only relevant USP Chapters and Board regulations, but also relevant provisions of federal law and related guidance documents, most notably the guidance documents released specific to bulk substances and insanitary conditions.

The committee has dedicated significant time to public discussion of outsourcing facilities operating under the authority of Section 503B for the FD&C Act and relevant sections of Pharmacy Law, as well as pharmacies compounding preparations pursuant to the authority of Section 503A of the FD&C Act relevant sections of Pharmacy Law and its regulations.

Both Pharmacy Law and federal law recognize the different requirements under which compounding must be performed in outsourcing facilities versus pharmacies, most notably that outsourcing facilities must perform compounding under current good manufacturing practices while compounding pharmacies follow 503A provisions, relevant USP Compounding Chapters and Board regulations.

During several meetings members have received public comment in support of compounded preparations provided by pharmacies using bulk ingredients that may not comply with legal provisions, including methylcobalamin. As discussed during these prior meetings, bulk substances such as methylcobalamin are generally graded as dietary grade or not graded at all. Use of such bulk ingredients in sterile compounded preparation could result in insanitary conditions.

Under the FDA's Interim Policy on Compounding Using Bulk Drug Substances under 503(A), the FDA provides that the FDA may not take enforcement action under specified conditions. It is important to note, as with all FDA guidance, the guidance is not binding on the FDA or the public. As staff understand the document, it is important to note that such conditions require evaluation but generally include:

1. The bulk substance appears in 503A Category I on FDA's website - - https://www.fda.gov/media/94164/download
2. The original manufacturer and all subsequent manufacturers of the bulk substance are establishments are registered under section 510 (including foreign establishments that are registered under section 510(i)) of the FD&C Act)
3. The bulk substance is accompanied by a valid COA; and
4. The product compounded using the bulk drug substance is compounded with all other conditions of section 503A of the FD&C Act. (Note: This would include compliance guidance related to insanitary conditions)

Further, the FDA reinforces the need for compounders to know bulk suppliers and confirm if such suppliers are testing the drugs before a compounder purchased bulk substances for patient use. In February 2021, the FDA posted an advisory, FDA to compounders: Know Your Bulks Supplier In this release the FDA noted several issues over the past few years related to repackagers of bulk drug substances, used in compounded drugs. The FDA has issued alerts about safety issues with various bulk substances, including highlighting concerns with using dietary ingredient glutathione to compound sterile injectables. Further, the FDA has issued warning letter to API repackagers for significant violations of CGMPs, including the warning letter issued to Professional Compounding Centers of America, dba PCCA, that was issued January 27, 2021, and briefly discussed at the January 2021 Board Meeting.

During the Committee's January 2021 meeting, members encouraged staff to continue to educate licensees about the provisions of law, the risks associated with compounding from an inappropriately graded material, and steps that could be taken to mitigate such risks. In addition, staff were directed to discuss the issue with the FDA and report back to the Committee.

Subsequent to the meeting, Board staff discussed the issue with the FDA, who confirmed that compounding from inappropriately graded products could result in violations of the guidance regarding insanitary conditions. The FDA indicated that such a determination is made considering a number of factors, including consideration of the bulk substances guidance document and insanitary conditions guidance document. As part of the discussion, FDA representatives also referred staff back to compounding risk alerts that have been issued by the FDA including the alert, FDA highlights concerns with using dietary ingredient glutathione to compound sterile injectables. The alert includes the following conclusions:

1. The powder the pharmacies received was labeled with "Caution: Dietary Supplement" and should not have been used to compound sterile injectable drugs. Ingredients not intended to use in compounding sterile injectable drugs can be harmful when administered to patients because they may contain impurities and contaminants, including endotoxins.
2. It is critical that compounders understand that quality should be built into the drug production, and that testing alone should not be relied on to ensure drug quality. Therefore, compounders

should ensure that all ingredients they use to produce sterile injectable drugs are manufactured under conditions and specifications appropriate for the intended route of administration.

3. FDA also urges manufacturers and repackagers to clearly label ingredients intended for use in dietary supplements. Additionally, repackagers should ask the manufacturer about the intended use of the ingredient. Clarifying information on the ingredient labels and in the COA could help prevent compounders from using ingredients not appropriate for compounding sterile injectable drugs.

As part of its ongoing activities, Board staff continue to educate licensees about the relevant provisions of law when identifying compounding with components or other materials that could result in insanitary conditions. Education typically focuses on provisions of the law, understanding the quality of the ingredient prior to use, understanding the testing specification and information included in the COA and possible implications to patients when impurities or other contaminants are identified, the importance of working with a supplier to improve the quality of bulk ingredients as well as the possible need to independently test bulk ingredients prior to use. Additionally, inspectors may provide several resources to licensees including:

1. "FDA to Compounders: Know Your Bulks Supplies", which states: "For patient safety and supply chain transparency, repackagers must follow all quality standards pertaining to them, including clearly identifying the original API manufacturer to their customers who use them to make the finished drugs patients take every day."

https://www.fda.gov/drugs/human-drug-compounding/fda-compounders-know-your-bulks-supplier

2. "Warning Letter: Professional Compounding Centers of America Inc. (PCCA)" (link below), for receiving and distributing adulterated and misbranded active pharmaceutical ingredients (APIs).

https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/warning-letters/professional-compounding-centers-america-dba-pcca-597638-01272021

3. "Guidance Document: Insanitary Conditions at Compounding Facilities" (link below). FDA defines *Insanitary conditions* as "conditions that could cause a drug to become contaminated with filth or rendered injurious to health. The drug itself need not actually be contaminated. A drug that is actually contaminated with any filthy, putrid, or decomposed substance is deemed to be adulterated under section 501(a)(1) of the FD&C Act (21 U.S.C. 351(a)(1))" One of the examples of Insanitary Conditions listed is following: "Using active ingredients, inactive ingredients, or processing aides, that have or may have higher levels of impurities compared to compendial or pharmaceutical grade equivalents (e.g., ingredients with potentially harmful impurities, ingredients labeled with "not for pharmaceutical use" or an equivalent statement)"

https://www.fda.gov/regulatory-information/search-fda-guidance-documents/insanitary-conditions-compounding-facilities-guidance-industry

4. "FDA highlights concerns with using dietary grade glutathione to compound sterile injectables" (link below). In the Conclusion portion of the letter it states, "It is critical that compounders understand that quality should be built into the drug production, and that testing alone should not be relied on to ensure drug quality. Therefore, compounders should ensure that all

ingredients they use to produce sterile injectable drugs are manufactured under conditions and specifications appropriate for the intended route of administration. FDA also urges manufacturers and repackagers to clearly label ingredients intended for use in dietary supplements. Additionally, repackagers should ask the manufacturer about the intended use of the ingredient. Clarifying information on ingredient labels and in the COA could help prevent compounders from using ingredients not appropriate for sterile injectable drugs.

https://www.fda.gov/drugs/human-drug-compounding/fda-highlights-concerns-using-dietary-ingredient-glutathione-compound-sterile-injectables

5. "USP – Guideline for assigning titles to USP Dietary Supplement Monographs" – See page 3 of this document. Specifically *"Paragraph 3(a) of DSHEA states that a DS shall be deemed to be a food (i.e., neither an over-the-counter nor prescription drug) within the meaning of this Act"*

https://www.usp.org/sites/default/files/usp/document/get-involved/submission-guidelines/guideline-for-assigning-titles-to-usp-dietary-supplement-monograph.pdf

6. "FDA Questions and Answers on Dietary Supplements" – ***"What is a dietary supplement?*** *Congress defined the term "dietary supplement" in the Dietary Supplement Health and Education Act (DSHEA) of 1994. A dietary supplement is a product taken by mouth that contains a "dietary ingredient" intended to supplement the diet. The "dietary ingredients" in these products may include: vitamins, minerals, herbs or other botanicals, amino acids, and substances such as enzymes, organ tissues, glandulars, and metabolites. Dietary supplements can also be extracts or concentrates, and may be found in many forms such as tablets, capsules, softgels, gelcaps, liquids, or powders. They can also be in other forms, such as a bar, but if they are, information on their label must not represent the product as a conventional food or a sole item of a meal or diet. Whatever their form may be, DSHEA places dietary supplements in a special category under the general umbrella of "foods," not drugs, and requires that every supplement be labeled a dietary supplement."*

https://www.fda.gov/food/information-consumers-using-dietary-supplements/questions-and-answers-dietary-supplements

Further, as part of its prior discussion, the Committee requested information on adverse events related to the use of methylcobalamin. Although the Board does not have access to Med Watch, the FDA maintains a public dashboard, FDA Adverse Events Reporting System. As indicated in the footnotes of this sytem, it is important to understand what the data includes, which is limited to voluntary direct reports submitted through the MedWatch program by consumers and healthcare professionals, mandatory reports and biological safety reports.

For Committee Discussion and Consideration

During the meeting members will have the opportunity to continue its discussion of the issue, including legal and safety issues.

e. Discussion and Consideration of Opportunities to Improve Naloxone Accessibility through Auxiliary Labels for Opioid Prescriptions

Relevant Law

Business and Professions Code (BPC) section 4076.7 requires that in addition to other labeling requirements, whenever a prescription drug containing an opioid is dispensed to a patient for outpatient use, the pharmacy or practitioner dispensing the drug shall prominently display on the label or container, a notice that states "Caution: Opioid. Risk of overdose and addiction."

BPC section 4052.01 established the authority for a pharmacy to furnish naloxone hydrochloride under specified conditions. Further, CCR section 1746.3, further defines that authority through regulation.

Background

July 23, 2020, the FDA issued a Drug Safety Communication recommending that health care professionals discuss the availability of naloxone, and consider prescribing it to patients who are at increased risk of opioid overdose. As part of the FDA News Release, FDA noted its work to help increase availability of naloxone and combat opioid overdoses.

As part of the October 27, 2020 Committee Meeting, members voted to agendize discussion of auxiliary labels used to assist with naloxone accessibility.

For Committee Consideration

During the meeting members will have the opportunity to discuss the issue and determine if any other action should be taken.

f. Discussion and Consideration of Assembly Bill 2789 (Wood, Chapter 438, Statutes of 2018) Health Care Practitioners: Prescriptions: Electronic Data Transmission

Relevant law

BPC section 688 establishes, on or after effective January 1, 2022, a requirement for health care practitioners (HCP) authorized to issue prescriptions to have the capability to transmit electronic data transmission prescriptions and would require pharmacies to have the capability to receive those transmissions. Further, this section provides several exceptions to the requirement. Specific exemptions include the following:

1. Prescriptions issued pursuant to HSC 11159.2.
2. An electronic data transmission is not available due to a failure of the computer system, application, or device; the loss of electrical power; or other service interruption.
3. The HCP is issuing a prescription to be dispensed by a pharmacy located outside of California
4. The prescription is issued in an ER or urgent care clinic and at least one of the following conditions are present.
    a. The patient resides outside of California.
    b. The patient resides outside of the geographic area of the hospital.
    c. The patient is homeless or indigent and does not have a preferred pharmacy.
    d. The prescription is issued when the patient's regular pharmacy is likely to be closed.
5. Prescriptions may be issued electronically, but do not require electronic transmission including:
    a. A prescription issued by a veterinarian.
    b. A prescription is for eyeglasses or contact lenses
    c. The prescribing HCP and dispenser are the same entity.
    d. The prescribing HCP determines such transmission would be impractical for the patient

to obtain the substance in a timely manner.

e. The prescription issued includes elements not covered by the latest version of the National Council for Prescription Drug Programs' SCRIPT standard

6. An HCP who does not transmit the prescription as an electronic data transmission shall document the reason in the patient's medical record within 72 hours of the end of the technological or electrical failure.
7. A pharmacy that receives the transmission but has not dispensed the medication shall, at the request of the patient or other authorized individual, immediately transfer or forward the electronic data transmission prescription to an alternative pharmacy.
8. If a pharmacy, or its staff, is aware that an attempted transmission of an electronic data transmission failed, is incomplete, or it otherwise not appropriately received, the pharmacy shall immediately notify the prescribing HCP.
9. A pharmacist who receives a written, oral, or faxed prescription shall not be required to verify that the prescription falls within one of the above exceptions and may continue to dispense medications from legally valid written, oral, or fax prescriptions.

For Committee Consideration and Discussion

During the meeting members will have the opportunity to discuss the provisions and hear from stakeholders to determine if, as part of its education on the requirements, development of Frequently Asked Questions, would be helpful.

g. Discussion and Consideration of Federal Food and Drug Administration Final Rule Related to Importation of Certain Canadian Prescriptions Drugs

Relevant Law

21 CFR Parts 1 and 251 include the final rule to implement a provision of the FD&A Act to allow for the importation of certain prescription drugs from Canada.

Background

In September 2020, the FDA and the Department of Health and Human Services announced a final rule to implement the provision of federal law that allows FDA-authorized programs to import certain prescription drugs from Canada under specific conditions.

In October 2020, the FDA released its guidance document on the Importation of Certain FDA – Approved Human Prescription Drugs, Including Biological Products, and Combination Products under Section 801(d)(1)(B) of the Federal Food, Drug, and Cosmetic Act.

For Committee Consideration and Discussion

As states begin to consider implementation of the requirements of the final rule and guidance documents, it appears appropriate to begin education of the federal requirements. During the meeting members will receive a brief overview of the federal rule. As part of its discussion members will have the opportunity to provide feedback to staff on any additional information that may be helpful to the Committee in future meetings, if appropriate.

A copy of presentation slides is provided in **Attachment 3**.

h. Summary of Presentation by the Office of the Attorney General on the Annual Report to the Legislature Pursuant to Business and Professions Code Section 312.2

Relevant Law
BPC section 312.2 requires the Attorney General to submit a report on an annual basis, specified data that includes summary enforcement related issues handled by the Office of the Attorney General.

For Committee Consideration and Discussion
During the meeting members will receive a presentation from Carl Sonne, Senior Assistant Attorney General on the summary information related to the Board.

A copy of presentation slides and relevant portion of the report is provided in **Attachment 4.**

i. Discussion and Consideration of Proposal to Develop an Alternative Enforcement Model

Relevant Law
BPC Section 4001.1 provides that protection of the public shall be the highest priority for the California State Board of Pharmacy in exercising its licensing, regulatory, and disciplinary functions. Further, the section states that whenever the protection of the public is inconsistent with other interests sought to be promoted, the protection of the public shall be paramount.

Article 19 (BPC sections 4300 – 4313), and other various provisions of Pharmacy Law and its regulation, define the provisions for disciplinary proceedings and other enforcement actions, acts that constitute unprofessional conduct and other violations of law, mitigating factors, and other authorizing and notification requirements.

CCR section 1760 requires the Board, when reaching a decision on a disciplinary matter, to consider the Disciplinary Guidelines, which are incorporated by reference into this regulation.

The Administrative Procedure Act (Government Code section 1140, et seq.,) defines the administrative case process developed to ensure due process.

Background
The Committee and Board have previously contemplated development of an alternative enforcement model. The goal of the alternative model is to reduce the time and cost associated with resolving a disciplinary matter which must be balanced with also continuing to provide due process to licensees, as well as consumer protection. The original proposal developed and considered by the Committee and Board was based on a model used by the Physical Therapy Board, that provides an option for pre-pleading settlement of an administrative matter where the outcome of the matter is a Public Letter of Reprimand. The language for such authority is provided below:

> **BPC 2660.3.**
> In lieu of filing or prosecuting a formal accusation against a licensee, the board may, upon stipulation or agreement by the licensee, issue a public letter of reprimand after it has conducted an investigation or inspection as provided for in this chapter. The public letter

> of reprimand may include a requirement for specified training or education, and cost recovery for investigative costs. The board shall notify the licensee of its intention to issue the letter 30 days before the intended issuance date of the letter. The licensee shall indicate in writing at least 15 days prior to the letter's intended issuance date whether he or she agrees to the issuance of the letter. The board, at its option, may extend the time within which the licensee may respond to its notification. If the licensee does not agree to the issuance of the letter, the board shall not issue the letter and may proceed to file the accusation. The board may use a public letter of reprimand only for minor violations, as defined by the board, committed by the licensee. A public letter of reprimand issued pursuant to this section shall be disclosed by the board to an inquiring member of the public and shall be posted on the board's Internet Web site.

Since its initial discussion, the Committee has considered various proposals to achieve the overall stated policy goals - - to reduce costs and case resolution time. As the various proposals have been considered, at times counsel has identified possible concerns, particularly with the involvement of Board Members as either part of the investigative or settlement process, as an example including Member(s) as part of a proposed oral conference as part of the alternative enforcement model.

Members have also reviewed statistical information regarding disciplinary cases including case outcome information, which indicates that in FY 2019/20, about 10% of all investigations resulted in referral of the matter to the Office of the Attorney General for possible disciplinary action. Additionally, of the administrative cases resolved, about 25 percent resulted in a default decision, 56 percent were resolved through a stipulated settlement, 10 percent were resolved through an administrative hearing and about 10 percent were withdrawn. When reviewing the outcome of the mail vote process, the Board voted to nonadopt less than 1 percent of stipulated settlements and about six percent of proposed decisions. Last, when evaluating the types of disciplinary outcomes about 30 percent result in revocation, which includes default decisions. In addition, about 23 percent result in the respondent voluntarily surrendering a license, about 30 percent result in a term of probation, and about 16 percent resulted in the license being publicly reproved.

Following discussion and consideration, including a proposal by stakeholders, the Committee directed staff to report back on possible solutions to meet the overall policy goal that do not require legislative changes. In preparation for this meeting staff have conferred with the Office of the Attorney General on possible changes that do not require legislative changes to implement. As part of this discussion, Board staff was advised about a pre-settlement conference used by the California Board of Accountancy, a brief description of which is provided below:

THE PRE-ACCUSATION REVIEW/CONFERENCE

> Before an accusation is filed, unless public safety requires immediate action, you may be offered an opportunity to review a draft accusation and comment on its factual content. The accusation will be available for review only at a scheduled pre-filing review conference. No copies will be released to you until the actual filing of the accusation.

Based on staff understanding of this conference, respondents are provided another opportunity to provide mitigation and/or rehabilitation for consideration by the Agency. Respondents are not required to participate in this conference. Information received during this conference could result in several outcomes including amendments to the draft pleading prior to filing or withdrawal of the matter. In addition, the pre-filing conference allows an opportunity to earlier engagement in

settlement where appropriate, which ultimately results in a reduction in resolution time. The Department of Managed Health Care (DMHC) uses its own Enforcement Division (as opposed to the Attorney General's Office) for resolution of its Enforcement Actions. As part of its process DMHC will sent a pre-accusation letter and allow the Licensee to response with information in its defense, or in mitigation. However, in the case of DMHC, if a settlement agreement is reached, the pre-accusation letter does not become public. If an agreement is not reached, a DMHC attorney will file an administrative accusation.

In addition, stakeholders were advised to contact the executive officer if interested in presenting a proposal to members during the April meeting.

For Committee Discussion

During this meeting members will have the opportunity to consider proposals from stakeholder as well as discuss the pre-filing conference model used by other agencies.

As members continue its discussion, it is suggested that the focus remain on the overall policy goal -- reducing costs and overall completion times. In addition, several policy questions should be considered including:

1. Is the proposed change consistent with the Board's consumer protection mandate?
2. Should the proposed change be limited to certain types of cases?
3. Would such changes provide the appropriate balance of consumer protection and due process?
4. Would such a change increase or decrease the time for case resolution?
5. What are potential impacts on cost is such changes were made.

Attachment 5 includes the current administrative case process flow chart.

j. Review and Discussion of Enforcement Statistics

Since July 1, the board received 1,601 complaints and has closed 1,777 investigations. The board has issued 186 Letters of Admonishment, 736 Citations and referred 133 cases to the Office of the Attorney General. The board has secured 11 interim suspension orders. Further, the board has revoked 55 licenses, accepted the disciplinary surrender of 62 licenses, denied 6 applications, and imposed other levels of discipline against 139 licensees and/or applicants.

As of April 1, 2021, the board has 1,324 field investigations pending. Below is a breakdown providing more detail in the various investigation process:

- 73 cases under review for assignment, averaging 13 days
- 572 cases under investigation, averaging 210 days
- 172 investigations under supervisor review, averaging 60 days
- 68 investigations under second level review, averaging 56 days
- 439 investigations waiting final closure (typically issuance of a citation or letter of admonishment) averaging 34 days

Attachment 6 includes the quarterly enforcement statistics.

k. Future Committee Meeting Dates

- July 15, 2021
- October 20, 2021

Attachment 1

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 Has Raised Questions Among Boards of Pharmacy

- What information will boards be required to collect and share with FDA?
- What mechanism will be used to collect, manage, and share information?
- What IT and personnel resources will be needed?
- Do "prescription orders" include new and refill prescription orders?
- Does the MOU apply to nuclear pharmacies?
- When does the "receipt of a complaint" by a board occur when there is an umbrella agency receiving complaints that board is not aware of right away?
- If a state is prohibited from reporting complaints under investigation, how can that state comply with the MOU?

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Additional Questions:

- If a state prohibits disclosure of a complainant's name, how can the board 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?
- The MOU's mandate to investigate complaints of adverse drug experiences and product quality issues related to compounded products may be interpreted to remove the state's discretion to determine if a complaint warrants investigation. Is this the case?
- How does a state handle a prescribing compounder who is distributing compounded drugs interstate?

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Additional Questions:

- What will FDA do with submitted information?
- When it comes to state investigations, can states leverage any FDA resources?
- What happens if a state doesn't comply with the MOU?
- Will FDA delay enforcement of the 5% rule due to COVID?
- What resources will the board need to expend to comply with the MOU?

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What Will Boards that Sign the MOU need to do?

- Investigate certain compounding pharmacy complaints
- Report certain compounding pharmacy and compounding physician complaints to FDA
- Report certain information about compounding physician offices
- Identify and report to FDA certain compounding pharmacy data

How will NABP's Information Sharing Network help?

- Provide a tool for states to report complaint information to FDA
- Provide a tool for states to review compounding pharmacy data and, if needed, report it to FDA

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What Specific Information Do Boards Need to Report?

- **Pharmacies** that are compounding human drug products **and distributing inordinate amounts interstate***, including their compounding data
- 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 human drug products **compounded by physicians**

*The distribution of inordinate amounts interstate is a threshold for the board of pharmacy to identify and report certain information to FDA, not a limit on the distribution of compounded products interstate.

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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 agrees the network will be a key to assisting boards in their efforts to comply with the MOU, understanding the lack of board resources
- FDA is eager to partner with NABP and boards to protect patients from high-risk compounders

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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 both boards and pharmacies to enter data
- Boards will be able to review information provided by licensees and upload documents, including complaints and inspection forms

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System Will Flag Compounding Pharmacy Data for States and 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 review and 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 for an identified calendar year:

- Name and address of state-licensed entity
- Whether the pharmacy participates in the following activities:
    - 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 (or caused to be sent out) of the facility (in state or out-of-state)
- Number of prescription orders for compounded drugs dispensed (e.g., picked up by the patient) at the facility
- Total number of prescription orders for compounded drugs sent out of 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 – What Information and When?

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 – What Information and When?

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 – What Information?

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 the following:

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 – When?

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 – What Information?

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 the following information, if available, 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 – When?

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. Pharmacy accreditation program applications (*except* for the DMEPOS program) and the VPP inspection application. The pharmacy will pay the regular accreditation or inspection application fee.
2. The pharmacy e-profile. New data fields are being added to pharmacy e-profiles. 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 Provide Requested Information?

- During the pilot project, all pharmacies submitting the requested data will have the opportunity to receive a VPP inspection at no cost to them.
- If a pharmacy pays for a VPP inspection or accreditation application and is selected to be surveyed under the pilot project, the cost of the survey will be refunded.

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Feedback from Boards

- Vast majority of boards are in the process of determining whether to sign the MOU.
- So far:
  - One state has signed the MOU
  - Seven have said they will sign the MOU pending some other needed action.
  - Eight states have said they cannot or will not sign the MOU, five due to technical or legal issues with the document. FDA would like to work with states that have expressed technical or legal issues.
- Some boards have said they do currently require pharmacies to submit this data to their own systems or are considering requiring pharmacies to report data to the system.
- NABP is in conversations with several boards about sharing compounding pharmacy data they already collect.

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Feedback from Profession

- NABP is working with pharmacy groups to help inform members about the MOU and the Information Sharing Network
  - Alliance for Pharmacy Compounding
  - National Home Infusion Association
  - PCCA

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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
- Map of state MOU decisions
- Slide deck

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Thank You!

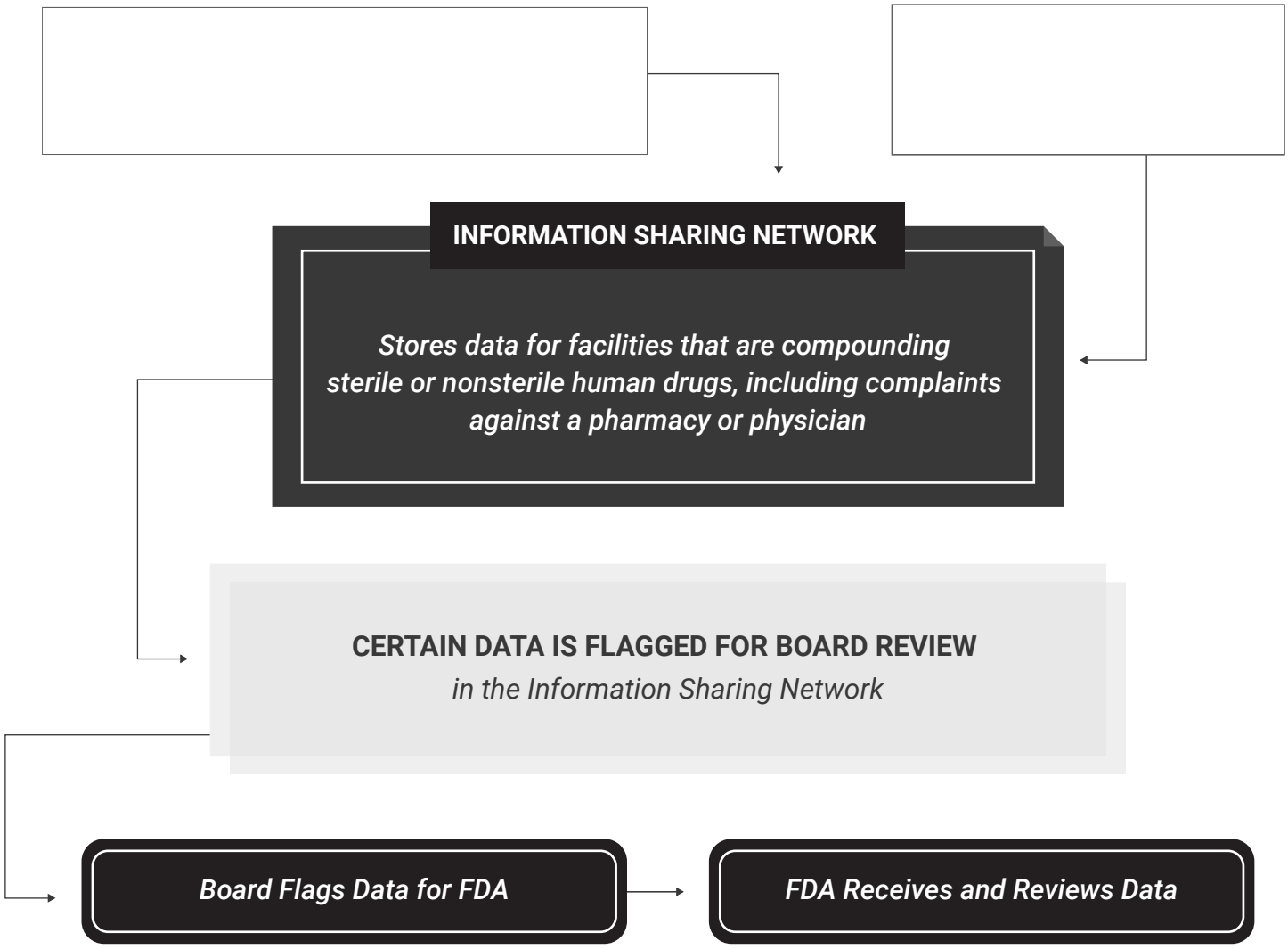
Collect and Share Compounding Data With NABP's Information Sharing Network

NABP's Information Sharing Network helps state boards of pharmacy collect, manage, and share data related to compounding pharmacies with Food and Drug Administration (FDA). Access to the network is free and allows your board to meet the obligations outlined in the memorandum of understanding (MOU) on compounded human drug products.

PATHWAYS FOR DATA ENTRY

& the flow of data through NABP e-Profile Connect

Developed as an expansion of NABP e-Profile Connect, the Information Sharing Network will be available for boards of pharmacy to begin entering data in early 2021.



Visit *www.nabp.pharmacy/Compounding-Project* for more information on how the Information Sharing Network works or to access the FDA MOU.

Data Collected

The Information Sharing Network collects the following pharmacy and complaint data.

General Pharmacy Information – Entered by the Pharmacy or the Board

- Name and address of state-licensed entity
- Whether the pharmacy participates in the following activities during an identified calendar year:
  - Human drug compounding — sterile or nonsterile
  - Patient-specific or non-patient-specific compounding
- If a pharmacy is compounding sterile or nonsterile human drug products, additional data is collected related to licensing, prescription orders, and distribution numbers

Complaint Information – Entered by the Board

Complaints of adverse drug experiences or product quality issues relating to human drug products that are compounded by a physician and distributed interstate are also entered by the board. Data collected includes:

- Name and contact information of the complainant or notifier
- Description of the complaint, including a description of any compounded human drug product that is the subject of the complaint
- The board's assessment of whether the complaint was substantiated, if available
- Description of any actions that the board has taken to address the complaint

Complaints of adverse drug experiences, product quality issues, or distribution of human drug products that are compounded by a physician are also entered by the board.

For a complete list of data collected in the Information Sharing Network, visit ***www.nabp.pharmacy/Compounding-Project.***

Data for Board Review

The Information Sharing Network flags data for the boards of pharmacy to review based on certain criteria.

- Pharmacies that are compounding human drug products and distributing inordinate amounts interstate.
- Complaints of serious adverse experiences or quality issues relating to drugs compounded by pharmacies and distributed interstate.
- Complaints of adverse experiences or quality issues relating to drugs compounded by a physician and distributed interstate.

By logging in to e-Profile Connect, the boards can review and submit the information to FDA with the click of a button.

Sending Data to FDA

Boards must submit the required information to FDA in accordance with the timelines outlined in the MOU, which can be as little as five days depending on the type of complaint.

A list of the data transmitted to FDA and the associated timelines can be found at *www.nabp.pharmacy/Compounding-Project.*

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Main Menu

Attention: NABP's e-Profile system will be unavailable due to system maintenance from 7-8 PM CDT on Wednesday, March 24, 2021. Thank you for your patience.

FDA Compounding MOU Project

Compounding Pharmacy Information Sharing Project

The Compounding Pharmacy Information Sharing Project was created in partnership with FDA to improve data sharing related to compounding pharmacies as outlined in the Memorandum of Understanding Addressing Certain Distributions of Compounded Human Drug Products (MOU).

As part of this project, NABP developed the Information Sharing Network to help state boards of pharmacy collect, manage, and share data related to compounding pharmacies with Food and Drug Administration (FDA) and meet the obligations of the MOU.

About the Project

Compounding Data Collection

Frequently Asked Questions

Understanding the MOU

FDA worked with NABP to develop a standard MOU for use by the state boards of pharmacy to aid with their compliance of section 503A(b)(3)(B)(i) of the Food, Drug and Cosmetic Act. As part of the MOU, boards must identify pharmacies that are compounding human drug products and distributing inordinate amounts of such products interstate and report those pharmacies to FDA. Boards can use the Information Sharing Network, accessible via e-Profile Connect, to meet the obligations outlined in the FDA MOU on compounded human drug products.

Learn more about the MOU and data collection for the project:

- Read the Compounding Pharmacy Information Sharing FAQs.
- Download our slide deck for details on preparing for the FDA MOU.
- Download the information sheet for a breakdown of the process for data entry and data flow through the Information Sharing Network.
- Contact prof-affairs@nabp.pharmacy if you have any additional

For more information about how the MOU can better position your board to address patient safety and improve communication between FDA and all boards of pharmacy, watch the recent webinar, *Preparing for FDA's Compounding MOU*.

Sign the FDA MOU

Meet MOU Obligations with the Information Sharing Network

Our Information Sharing Network makes it easy to report and review data about pharmacies compounding sterile or nonsterile human drugs, as well as complaints against a pharmacy or physician.

While signing the MOU does not require boards to enter data into the network, boards are encouraged to use the Information Sharing Network to create a uniform and streamlined reporting process with FDA. Boards can rely exclusively on the data reported through the network and easily transmit data to FDA electronically.

Easy Access to Data

All boards can access data in the Information Sharing Network by logging in to NABP e-Profile Connect.

Reduced Administration Burden

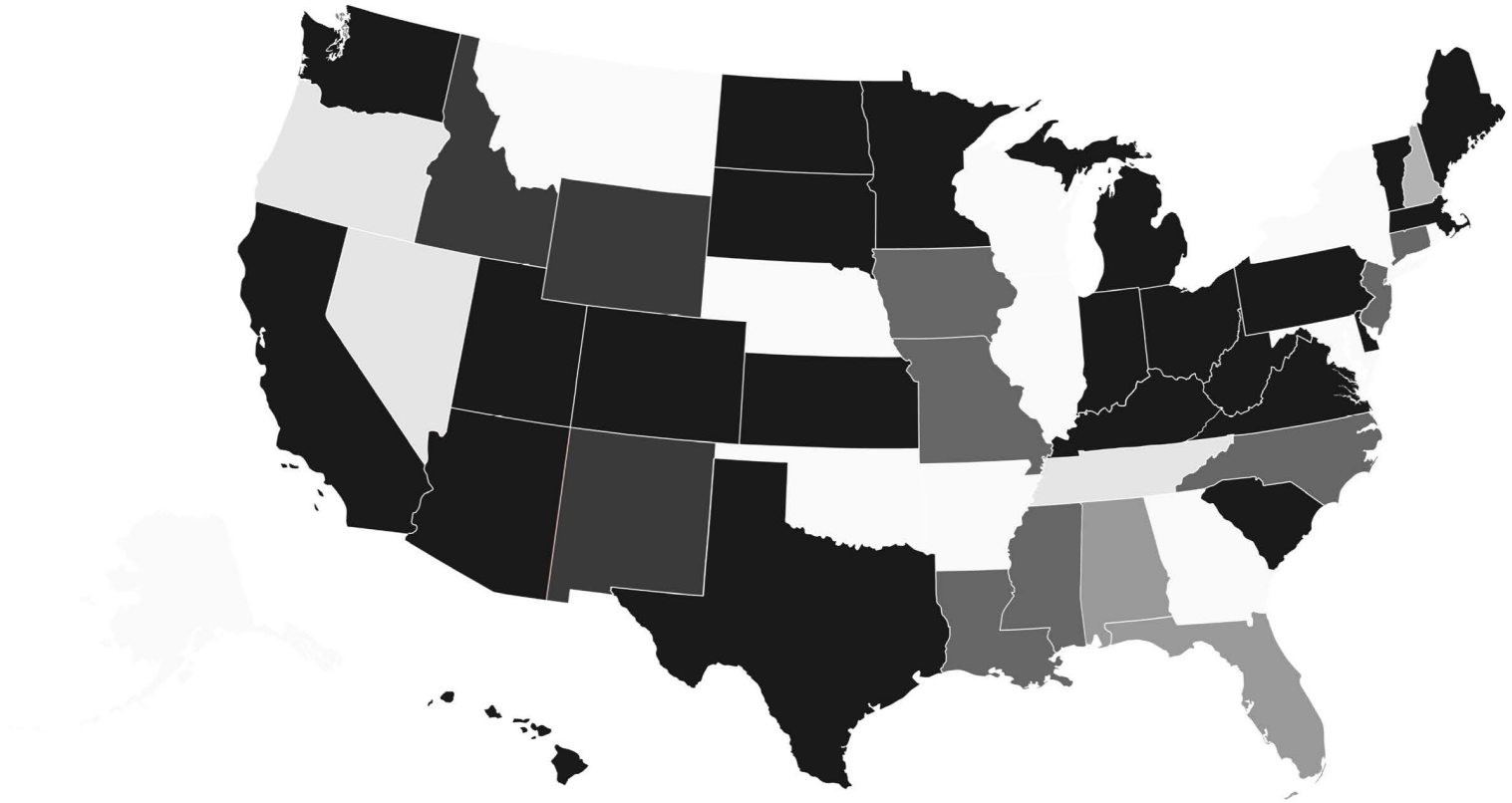
Compounding data is collected in the facility e-Profile, and will soon be collected on certain accreditation and the VPP application, and appears automatically in the system for board review, helping to reduce the amount of data entry required by the boards.

Simple Submission Process

Boards can review and submit data to FDA with the click of a button.

The Information Sharing Network is hosted in NABP e-Profile Connect, which has been expanded to accommodate the collection of compounding pharmacy data. Data in the system is accessible to all boards, even if they have not signed the MOU.

MOU PARTICIPATION



Yes | Yes, Pending Additional Action | Considering Signing

No | No, Due to Legal or Technical Reasons | No, Due to Legal or Technical Reasons. Considering Regulation

April 7, 2021

Attachment 2

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).

Memorandum of Understanding Addressing Certain Distributions of Compounded Drugs: Questions and Answers

FDA is working to respond to questions from states regarding the Memorandum of Understanding Addressing Certain Distributions of Compounded Human Drug Products (/media/143283/download) between state boards of pharmacy or other state agencies and FDA. This web page will be updated as we receive additional questions. Please email questions to compounding@fda.hhs.gov (mailto:compounding@fda.hhs.gov).

1. **Will states have an opportunity to negotiate the language of the MOU?**

   No. FDA has made the standard MOU available for signature. Section 503A of the FD&C Act directs FDA to develop, in consultation with the National Association of Boards of Pharmacy (NABP), a standard MOU for use by states. Developing individualized MOUs would create a patchwork of regulation of distribution of compounded drugs interstate and it would be impractical to have individual MOUs with each state.

   The MOU describes, in brackets, the state in the agreement as "State Board of Pharmacy or other appropriate State agency." The bracketed language appearing in the MOU is intended to be substituted with the appropriate name and contact information of the state.

2. **Can the state solely rely on pharmacies entering information into an information sharing network to identify pharmacies that distribute inordinate amounts of compounded human drug products interstate under the MOU?**

   By signing the MOU, the state is agreeing to identify pharmacies that distribute inordinate amounts of compounded drugs interstate. However, the MOU provides flexibility in how the state does this, including use of tools like an information sharing network, such as the one established in cooperation with NABP. If a state that chooses to use an information sharing network is uncertain whether the information it contains is complete, the state may verify information through other means, such as during inspections. FDA will continue to work with states to address questions regarding reporting expectations under the MOU.

3. **What will FDA do with information submitted by the states under the MOU?**

   Protecting patients is our top priority. Information submitted by the states will help inform FDA about potential for patient harm, including whether additional federal oversight is warranted. The information submitted by the states also will help inform the agency's risk-based inspection priorities.

4. **What happens if a state does not fulfil the agreements under the MOU?**

   The MOU may be terminated upon a 60-calendar day notice of termination if a state does not adhere to the MOU provisions.

5. **Can states use their established processes to investigate complaints of adverse drug experiences and drug quality issues?**

Yes, states can use their established processes as long as those policies and procedures do not conflict with the terms of the standard MOU. The MOU indicates any state investigation will be performed according to the state agency's established investigatory policies and procedures, including those related to prioritizing complaints.

For example, using established procedures, a state board of pharmacy or other appropriate state agency may review an incoming complaint describing an adverse drug experience and determine the complaint does not warrant further investigation. In other cases, a state board of pharmacy or other appropriate state agency may determine that an incoming complaint contains insufficient information and investigate further to determine appropriate action.

Draft Statutory Proposal Related to the Interstate Distribution of Compounded Medications

Amend Section 4110 of the Business and Professions Code as follows:

4110.(a) License Required; Temporary Permit Upon Transfer of Ownership; Mobile Pharmacy Requirements (a) No person shall conduct a pharmacy in the State of California unless he or she has obtained a license from the board. A license shall be required for each pharmacy owned or operated by a specific person. A separate license shall be required for each of the premises of any person operating a pharmacy in more than one location. The license shall be renewed annually and shall include the matters identified by the board in the renewal application, including but not limited to, notification to the board regarding compounding practices, including compounded prescriptions distributed outside of the State. The board may, by regulation, determine the circumstances under which a license may be transferred.

(b) …

Add Section 4126.9 to the Business and Professions Code as follows:

4216.9 Distribution of Compounded Drugs in Interstate Commerce by Pharmacies Located in California

a) A pharmacy located in California may only distribute compounded preparations for interstate distribution under the following conditions.

1. Between January 1 and March 31 of each year, report all required data into the Information Sharing Network established by the National Association of Boards of Pharmacy in conjunction with the federal Food and Drug Administration (FDA) to implement the Memorandum of Understanding established by the FDA Addressing Certain Distributions of Compounded Drugs.
2. On an annual basis, as a condition of renewal, the pharmacist-in-charge certifies that the reporting requirements established in section 1 have been satisfied.
3. Adverse drug experiences and product quality issues for all compounded products shall be reported to the board within 12 hours.

b) Confidential Treatment of Information Reported to the FDA Directly or Through the Information Sharing Network. All information reported by the board to the FDA directly or through the Information Sharing Network established in conjunction with the FDA is deemed to be confidential information as specified in California Government Code § 6254(f) if it relates to information regarding a complaint received or the investigation of any such complaint.

alliance for natural health USA

Alliance for Natural Health USA
1011 E Jefferson St #204
Charlottesville, VA 22902
(800) 230-2762
www.anh-usa.org

February 22, 2021

To the members of the California State Board of Pharmacy:

On behalf of the Alliance for Natural Health USA (ANH), I am writing to urge you to seriously consider deep flaws with the FDA's Memorandum of Understanding concerning compounded medications, and to contact the agency with your concerns.

ANH is a nonprofit organization representing one million consumers and healthcare practitioners across the U.S. ANH protects the right of natural health practitioners to practice, and the right of consumers to choose the healthcare options and treatment modalities they prefer, including complementary and alternative medicine. We believe a system that is single-mindedly focused on "treating" sick people with expensive drugs, rather than maintaining healthy people, is neither practical nor economically sustainable.

Compounded medications are a key component of natural healthcare, as they are tailored to individual patient needs.

I'm writing to tell you that your decision, as the state board of pharmacy, about whether to sign FDA's Memorandum of Understanding with states has potentially catastrophic implications for access to compounded medications in your state.

The MOU has serious flaws. It conflates definitions of 'distribute' and 'dispense' in a way Congress never anticipated. As a result, in states that sign the MOU, FDA will gain oversight of certain aspects of traditional dispensing, which has long been the purview of state boards of pharmacy, NOT a federal agency. In addition, FDA seriously underestimated the administrative burden on state boards that sign the MOU – the costs of staffing, reporting, etc. required of states in order to comply. The MOU creates, in effect, an unfunded mandate on states that sign.

But there are also problems – potentially greater ones – for states that DON'T sign:

If your state board does not sign the MOU, compounding pharmacies will be limited to shipping NO MORE THAN 5% of compounded preparations out of state. For many, many compounders, that 5% cap will impede countless patients from getting their medications. It could well put some compounders out of business and result in lost jobs (and tax revenue) in your state. That's an unfortunate position state boards of pharmacy have been put in by FDA – making a decision that could hurt

local economies, not to mention patient care. (This 2020 op-ed by Virginia Congressman Morgan Griffith makes that point well.)

I urge you to consult with compounding pharmacy owners. The MOU is deeply flawed, and both NABP and FDA need to hear from you about your concerns now, not later. If they don't hear from you, there's no chance the MOU can be amended and improved. So please write to NABP and FDA.

What happens if FDA is unwilling to make changes? I'll be asking you to sign the MOU because that 5% cap on out-of-state shipments that will be imposed if you don't sign will be the death knell for many compounders. I do understand your role as a regulatory agency is to protect consumers. But when pharmacies can't stay in business, patients in-state and out-of-state can't access the medications they need. How does that protect consumers?

Thank you for your consideration.

Sincerely,

Gretchen DuBeau, Esq.
Executive and Legal Director
Alliance for Natural Health USA

April 19, 2021

California Board of Pharmacy
2720 Gateway Oaks Drive, Suite 100
Sacramento, CA 95833

RE: Consideration for Signing FDA's Memorandum of Understanding

McGUFF COMPOUNDING PHARMACY SERVICES, INC.

Dear California Board of Pharmacy Enforcement Committee,

McGuff Compounding Pharmacy Services, Inc. (CPS), serving thousands of patients across 48 states, is concerned about the Memorandum of Understanding (MOU) that the Food and Drug Administration (FDA) finalized in October of 2020.[1] CPS understands the document is inherently flawed in that it leaves individual states to investigate and respond to complaints related to compounded human drug products and to monitor interstate distribution of inordinate amounts of compounded human drug products. There are also administrative burdens placed squarely on the California State Board of Pharmacy (the Board) with related costs incurred to the state to carry out the various reporting tasks required by the MOU. However, we strongly believe that for the following reasons, by not signing the MOU, the health and safety of Californians will be jeopardized and in-state California pharmacies harmed.

1. ***California Compound Quality Standards Exceed Other States:***
   Thanks to the Board's strong efforts in advocating for patient safety concerning pharmaceutical compounds, California has some of the highest quality expectations for compounded drugs in the country. This is reflected in the state's compounding regulations, which meet and often exceed the minimum standards required by the United States Pharmacopoeia (USP) chapters <795> and <797>.[2, 3, 4] For perspective, in 2018, Pew Charitable Trusts reported that California was one of only ten states having strong standards for sterile compounding practices that are equivalent or stricter than USP <797>.[5] Therefore, it can be argued that preparations compounded by pharmacies in California achieve a higher level of quality over compounds prepared in most other states.

2. ***503B Outsourcing Facilities are Not the Complete Answer to Interstate Commerce of Compounded Drugs:***
   The Board and the FDA may prefer patients obtain sterile compounds from FDA registered 503B facilities, however there are currently only 29 outsourcing facilities actively licensed by the California Board of Pharmacy out of the 69 503B outsourcing facilities currently registered with the FDA.[6, 7, 8] As per an outsourcing facility product report search, each of the facilities licensed in California focusses on manufacturing select therapeutic specialty compounds and do not offer wide-ranging product lines to meet the needs of every unique patient.[9, 13]

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Section 503B(d)(4) of the FD&C Act defines an outsourcing facility as a facility at one geographic location that is engaged in compounding sterile drugs.[10] As such, access to non-sterile compounds are often limited to coming from 503A pharmacies.

While 503B outsourcing facilities are key to mass-producing quality compounds, they are limited to the Category 1 list for the bulk drug substances they can use to prepare finished compounds or face mass-production challenges and limitations in compounding with FDA approved drugs as starting materials.[11] Whereas 503A pharmacies can prepare compounds with bulk active ingredients having a USP-NF monograph, those that are found in FDA approved drugs, and those on the Category 1 bulks list.[12] Therefore, signing the MOU is critical to maintaining patient access to compounded medications that can only come from 503A pharmacies.

In 2019, the Office of Inspector General reported that 44.8% of hospitals surveyed faced challenges in obtaining all the non-patient-specific drugs they sought from 503B outsourcing facilities. It was also found that 55.8% of hospitals that obtained non-patient-specific drugs from outside compounders relied on more than one facility for locating compounded medications. The report additionally revealed that hospital's needs are not being met by outsourcing facilities to effectively serve drug shortages.[13]

These findings collectively reiterate the importance of maintaining access to various compounds across numerous specialties with the help of 503A compounding pharmacies. Therefore, to maintain national patient access to various medications from 503B outsourcing facilities as well as from 503A pharmacies, CPS encourages all states, and particularly California, to sign the MOU. As of March 18, 2021, the NABP reports that 42% of the country is considering signing the MOU.[14] Given the propensity for California to be a leading force in shaping national public policies, if California signs the MOU, it's possible the nation will follow. Conversely, if California does not sign, it's also possible the nation will follow.

3. A Centralized System for Tracking Complaints and Interstate Commerce of Compounds will Enhance Patient Safety:

It is the FDA's intention that a MOU be signed by all states so that entities that ship compounds across state lines can be regulated appropriately.[1] The MOU also requires the states to track and respond to complaints related to compounded human drug products. If California does not sign the MOU, then pharmacies will be allowed to ship 5% of compounds across state lines. Additionally, a pharmacy complaint tracking system will likely continue to be lacking. If 503A entities are not appropriately regulated and tracked for compliance and quality, patient safety could be compromised in pharmacies that fall under the 5% threshold. Given the New England Compounding Center's and other past compounding-related

tragedies as well as the Board's evident intent to maintain patient safety, it makes sense that the Board would want to sign the MOU since these ideologies align.[15]

4. ***Maintain 503A Pharmacies as a Part of the National Emergency Solution:***
   Since the COVID-19 pandemic began in 2020, the nation witnessed a disruption in a drug supply chain that is already constantly taxed with numerous drug shortages.[16, 17] In response, the FDA granted temporary guidance documents allowing 503A pharmacies flexibility for assisting pharmaceutical manufacturers and 503Bs in maintaining the drug supply chain.[18, 19] If California (and other states) do not sign the MOU, pharmacies will not obtain out-of-state licenses in the first place and will not be ready for aiding the next widespread national crisis.

5. ***Maintain a Safe and Fair Marketplace in California:***
   The California Department of Consumer Affairs mission is as follows,

> ***"We protect California consumers by providing a safe and fair marketplace through oversight, enforcement, and licensure of professions."***
>
> -California Department of Consumer Affairs

The California Board of Pharmacy mission is as follows,

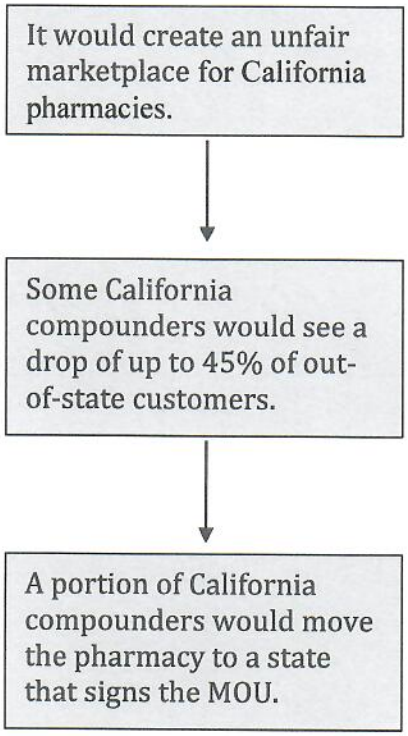
> ***"The Board of Pharmacy protects and promotes the health and safety of Californians by pursuing the highest quality of pharmacist's care and the appropriate use of pharmaceuticals through education, communication, licensing, legislation, regulation, and enforcement."***
>
> -California Board of Pharmacy

The MOU as written does not restrict reciprocity of the 5% rule, meaning if California chooses not to sign the MOU, the same 5% restriction into California does not apply for other states that do sign it.[1] This means if California does not sign the MOU and for example Texas does, California would likely see a drop in in-state-compounded preparations with an increase in compounds being shipped into California from Texas (see Figure).

This is because a portion of resident compounders would likely be lost to other states that sign the MOU to prevent losing up to 45% of their patients by staying in California.[1] This is also because some California pharmacies would likely close down altogether due to an unfair marketplace practice not imposed by other states that sign the MOU. As a result, a fiscal impact analysis would likely see a decrease in resident pharmacy and sterile compounding license fee revenues as well as a decrease in the California state tax base. Non-resident license fee

revenues may decrease from other states if those locations follow California's lead in not signing the MOU or if the Board restricts out-of-state pharmacy licenses to maintain a fair marketplace in California. In this scenario, California would also lose access to unique compounds prepared in non-resident pharmacies which are not made by resident pharmacies. Conversely, non-resident license fee revenues may increase in those states that do decide to sign the MOU and if the Board does not restrict out-of-state licensees. In that scenario, there would be fewer quality compounders residing in California and additional non-resident compounders, putting the burden on Board inspectors to perform many more out-of-state sterile compounding license inspections over in-state inspections.

Figure 1: What Happens if the Board Does NOT Sign the MOU?



If other states follow California and do not sign the MOU or if the Board restricts out-of-state pharmacy licenses to maintain a fair marketplace.

Fiscal Outcome	Health Outcome
A decrease in resident pharmacy & sterile compounding license fee revenues, a decrease in the California state tax base, and a decrease in non-resident license fee revenues.	A decrease in patient access to compounds prepared in resident and non-resident pharmacies.

If the Board does not restrict out-of-state pharmacy licenses.

Fiscal Outcome	Health Outcome	New Burden
A decrease in resident pharmacy & sterile compounding license fee revenues, a decrease in the California state tax base, and an increase in non-resident license fee revenues.	A decrease in patient access to compounds prepared in [quality] resident pharmacies and an increase from non-resident pharmacies.	An increase in out-of-state sterile compounding license inspections.

Since California is among the minority of states having strong standards for sterile compounding practices that are equivalent or stricter than USP <797>,[5] preparations compounded by pharmacies in California may achieve a higher level of quality over those prepared in other states. Therefore, in order to protect and promote the health and safety of Californians, CPS requests the Board consider signing the MOU.

6. ***Maintain Patient Mobile Lifestyles and Consistent Pharmacy Access for Better Health Outcomes:***

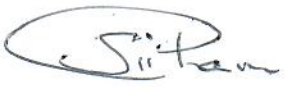
   Several technological advances have made today's modern world smaller than ever. People may live in one state, work in another, have bi-coastal living schedules, reside near state lines, or in states that lack numerous compounding pharmacy choices. Patients want to maintain consistent access to their prescriptions with the professionals and facilities they have developed a relationship. Health outcomes fare better when a patient's healthcare team is consistent. Not signing the MOU will discourage continuity of care for many patients, which may negatively affect their health outcomes.

For the reasons stated above, CPS urgently believes that patients and prescribers residing both outside and within California would prefer and benefit from having continued access to compounds produced and dispensed to them from California pharmacies. To test our belief, on April 5, 2021, CPS distributed a petition to patients and providers throughout the 48 states it serves, to ask the California Board of Pharmacy to sign the MOU. Within 10 days, CPS received an overwhelmingly positive response for California to sign the MOU. Specifically, CPS received 1,682 signatures from patients and providers outside of California and 1,053 signatures from those residing within California. We expect this number to grow as time goes by.

CPS realizes there is no easy answer in solving this problem and wants to help the Board find a resolution to this matter. One option for funding the reporting task would be to raise the sterile compounding license fee and instill reinspection fees on facilities that are not compliant with regulations and that prompt additional inspections. Another option would be to model the reporting system after the product reporting systems and adverse event reporting systems imposed on 503Bs and pharmaceutical manufacturers by the FDA.

Thank you for your consideration. We invite the Board at its preference to discuss with us further, and look forward to participating in all future conversations regarding this matter.

Respectfully,



Si Pham, Pharm. D.
Pharmacist-in-Charge
McGuff Compounding Pharmacy Services, Inc.

References:

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2. Title 16 California Code of Regulations (CCR), §1735 Compounding in Licensed Pharmacies, and §1751 Sterile Compounding.
3. <795> *Pharmaceutical Compounding—Nonsterile Preparations*. United States Pharmacopeial Convention, Rockville, MD.
4. <797> *Pharmaceutical Compounding – Sterile Preparations*. United States Pharmacopeial Convention, Rockville, MD.
5. The Pew Charitable Trusts and the National Association of Boards of Pharmacy. (2018, February). *State Oversight of Drug Compounding*. Retrieved April 2, 2021 from https://www.pewtrusts.org/-/media/assets/2018/02/drug_safety_assesment_web.pdf.
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