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State of New Hampshire

OFFICE OF PROFESSIONAL LICENSURE AND CERTIFICATION
DIVISION OF ADMINISTRATION
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Lindsey B. Courtney
Executive Director

March 25, 2021

His Excellency, Governor Christopher T. Sununu
and the Honorable Council
State House
Concord, New Hampshire 03301

REQUESTED ACTION

Authorize the Office of Professional Licensure and Certification (OPLC) to enter into a Memorandum of Understanding (MOU) with the U.S. Food and Drug Administration (FDA) regarding the distribution of inordinate amounts of compounded human drug products interstate and the appropriate investigation by the OPLC of complaints relating to human drug products compounded in the State of New Hampshire ("State") and distributed outside such State. This MOU is 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. Effective upon Governor and Council approval until terminated by either party.

EXPLANATION

OPLC is statutorily required, pursuant to RSA chapter 318 and the Federal Regulations noted above to regulate and ensure the safety of compounded human prescription drug products in the State of New Hampshire. The U.S. FDA requires state agencies which regulate these products to enter into an MOU where the expectations of each party are clearly delineated. As OPLC already performs the inspection of New Hampshire pharmacies and drug manufacturers where compounding takes place, there is no fiscal impact to the State by entering into this agreement.

Respectfully submitted,

LBCourtney

Lindsey B. Courtney
Executive Director

MEMORANDUM OF UNDERSTANDING ADDRESSING CERTAIN DISTRIBUTIONS OF COMPOUNDED HUMAN DRUG PRODUCTS BETWEEN THE NEW HAMPSHIRE OFFICE OF PROFESSIONAL LICENSURE AND CERTIFICATION AND THE U.S. FOOD AND DRUG ADMINISTRATION

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number. The OMB control number for this information collection is 0910-0800 (expires 10/31/2023).

I. PURPOSE

This Memorandum of Understanding (MOU) establishes an agreement between the New Hampshire Office of Professional Licensure and Certification (OPLC) 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 OPLC of complaints relating to human drug products compounded in the State of New Hampshire ("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 OPLC 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 Office of Professional Licensure and Certification will investigate complaints of adverse drug experiences and product quality issues[4] relating to human drug products compounded at a pharmacy in the State of New Hampshire and distributed outside the State. Any investigations will be performed pursuant to the New Hampshire Board of Pharmacy's (NHBOP) or OPLC'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 Board or OPLC 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 investigation, if the complaint is substantiated, the New Hampshire Board of Pharmacy, in accordance with and as permitted by State law, will take the action that the New Hampshire Board of Pharmacy 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 OPLC 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 OPLC receives notice of the complaint. The OPLC 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 OPLC 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 New Hampshire Board of Pharmacy or the OPLC 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 OPLC 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 OPLC 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 OPLC will notify the appropriate regulator of physicians within the State. The OPLC 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) New Hampshire Board of Pharmacy's assessment of whether the complaint was substantiated, if available; and (ii) Description and date of any actions the NHBOP has taken to address the complaint.

[8] The distribution of inordinate amounts of compounded human drug products interstate is a threshold for the NHBOP 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

$$\frac{AA}{BB} = XX, \text{where:}$$

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 OPLC and/or NHBOP will identify, using surveys, reviews of records during inspections, data submitted to an Information Sharing Network, or other mechanisms available to the OPLC and/or NHBOP, 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 OPLC and/or NHBOP 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 OPLC 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 OPLC becomes aware of a physician who is distributing any amount of compounded human drug products interstate, the OPLC will notify the appropriate regulator of physicians within the State. The OPLC 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. NHBOP's assessment of whether the complaint was substantiated, if available; and

      v. Description and date of any actions the NHBOP 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 OPLC 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 OPLC 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 OPLC and/or NHBOP 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 OPLC and/or NHBOP 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 OPLC and NHBOP affirm 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 OPLC and NHBOP no longer have the legal authority or resources necessary to effectively carry out all aspects of this MOU, the OPLC 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

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Authorized Representative of the New Hampshire Board of Pharmacy
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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 OPLC and/or NHBOP do 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 OPLC and/or NHBOP 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 Office of Professional Licensure and Certification New Hampshire Board of Pharmacy
By: Amy P. Abernethy, M.D., Ph.D.	By: Lindsey B. Courtney
Title: Principal Deputy Commissioner Food and Drug Administration	Title: Executive Director, Office of Professional Licensure and Certification & Authorized Representative of the New Hampshire Board of Pharmacy
Date: 03/18/2021	Date: 12/4/20
Amy P. Abernethy -S Digitally signed by Amy P. Abernethy -S Date: 2021.03.18 15:28:23 -04'00'	

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).