DRAFT MEMORANDUM OF UNDERSTANDING ADDRESSING CERTAIN DISTRIBUTIONS OF COMPOUNDED HUMAN DRUG PRODUCTS BETWEEN THE STATE OF [insert STATE] AND THE U.S. FOOD AND DRUG ADMINISTRATION

I. PURPOSE

This Memorandum of Understanding (MOU) establishes an agreement between the State of [insert State] and 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 State of [insert State] of complaints relating to compounded human drug products distributed outside such State. 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 drugs that are compounded by registered outsourcing facilities.

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 (CGMP) (section 501(a)(2)(B) (21 U.S.C. 351(a)(2)(B));

   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, among other things, a compounded human drug product must meet the condition 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[1] of compounded human drug products interstate and provides for appropriate investigation by a State agency of complaints relating to compounded human drug products distributed outside such State (section 503A(b)(3)(B)(i)); or

[1]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 a of commercially available drug product).

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 human 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 for use by the States in complying with section 503A(b)(3)(B)(i). The content of this MOU conforms with 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. Appropriate agencies of the State of [insert State] will investigate complaints received relating to human drug products compounded by a pharmacist, pharmacy, or physician located in the State of [insert State] and distributed outside the State. Primary responsibility for investigating complaints involving human drug products compounded by a pharmacy or pharmacist will generally lie with the [insert State Board of Pharmacy or other appropriate State agency] and similar responsibility for human drug products compounded by a physician will generally lie with the [insert State Medical Licensing Board or other appropriate State agency], except where State laws otherwise require. The [insert State Board of Pharmacy or other appropriate State agency] and [insert State Medical Licensing Board or other appropriate State agency] will cooperate in investigating any complaints involving overlapping jurisdiction.

2. Complaints relating to compounded human drug products distributed outside the State that will be investigated include reports received by the State concerning adverse drug experiences, or product quality issues that if left uncorrected could lead to potential public health risks or safety concerns. See Appendix A for definitions of *adverse drug experiences* and *product quality issues*.

3. Any investigations performed by the State of [insert State] under this MOU will include, but are not limited to (1) determination of whether there is a potential public health risk or safety concern associated with the compounded human drug product; and (2) confirmation that any risk or safety concern associated with the product is adequately contained (i.e., there is no ongoing risk to the public).

4. Based on findings from an investigation of a complaint about compounded human drug products distributed outside the State, if the complaint is found to be valid, the State of [insert State], in accordance with State law, will take appropriate action to ensure that the relevant compounding pharmacist, pharmacy, or physician determines the root cause of the problem that is the subject of the complaint and undertakes sufficient corrective action to eliminate any identified public health risk relating to the complaint, including the risk that future similar complaints may occur.

5. The State of [insert State] will notify FDA by sending an e-mail to StateMOU@fda.hhs.gov (see section III.c.1 of this MOU) within 72 hours of receiving any complaint relating to a compounded human drug product distributed outside the State involving a public health risk or immediate safety concern, such as a report of a serious adverse drug experience or serious product quality issue. The notification will include the State's initial assessment of the validity of the complaint relating to a compounded human drug product distributed outside the State, as well as a description of any actions the State has taken or plans to take to address such complaints. See Appendix A for definitions of *serious adverse drug experience* and *serious product quality issue*.

6. The State of [insert State] will maintain records of the complaint, the investigation of the complaint, and any response to or action taken as a result of the complaint, beginning when the State receives notice of the complaint. The State 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.

b. Distribution of Inordinate Amounts of Compounded Human Drug Products Interstate

1. The State of [insert State] will review compounding records during inspections of compounding pharmacies to identify whether the compounding pharmacy, or the compounding pharmacist or physician, is distributing inordinate amounts of compounded human drug products interstate. See Appendix A for the definition of *distribution*.

2. The State of [insert State] will notify FDA by sending an e-mail to StateMOU@fda.hhs.gov (see section III.c.1 of this MOU) within 7 days of identifying a pharmacist, pharmacy, or physician within its jurisdiction that has distributed inordinate amounts of compounded human drug products interstate.

3. The State of [insert State] will take action regarding any pharmacy, pharmacist, or physician that distributes inordinate amounts of

compounded human drug products interstate. State action may include a warning letter, enforcement action, suspension or revocation of a license, or other action consistent with State law. FDA may also take action regarding any pharmacy, pharmacist, or physician that distributes inordinate amounts of compounded human drug products interstate.

4. For purposes of this MOU, a pharmacist, pharmacy, or physician has distributed an inordinate amount of compounded human drug products interstate if the number of units of compounded human drug products distributed interstate during any calendar month is equal to or greater than 30 percent of the number of units of compounded and non-compounded drug products distributed or dispensed both intrastate and interstate by such pharmacist, pharmacy, or physician during that month. Exception: For purposes of this MOU, FDA does not intend to include, in the consideration of inordinate amounts, prescriptions dispensed to a patient (or patient's agent), if the patient (or patient's agent) to whom the drug is dispensed carries the drug across State lines after it has been dispensed to the patient (or patient's agent) at the facility in which the drug was compounded.

c. Submission and Disclosure of Information

1. When submitting information to StateMOU@fda.hhs.gov regarding complaints relating to compounded drug products distributed outside the State or distribution of inordinate amounts of drugs interstate, the following minimum information will be included:

- Name and contact information of the complainant, in the case of a complaint;
- Name and address of the pharmacist/pharmacy/physician that is the subject of the complaint or distribution in inordinate amounts;
- Description of the complaint, or description of the evidence indicating that the pharmacist/pharmacy/physician has distributed inordinate amounts of compounded human drug products interstate, including a description of any compounded drug product that is the subject of the complaint or distribution;
- State's initial assessment of the validity of the complaint relating to a compounded human drug product distributed outside the State; and

- Description and date of any actions the State has taken to address the complaint or the distribution of inordinate amounts of compounded human drug products interstate.

2. 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 or commissioning of officials under 21 CFR 20.84 may be necessary before FDA can share information that is protected from public disclosure. Such an agreement, or commissioning terms, will govern FDA's sharing of the following types of information:

   - confidential commercial information, such as the 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., Trade Secrets Act (18 U.S.C. 1905)), the Privacy Act (5 U.S.C. 552a), other Freedom of Information Act exemptions not mentioned above (5 U.S.C. 552(b)), the FD&C Act (21 U.S.C. 301 et seq.), 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 State of [insert State] will only be disclosed consistent with applicable federal law and regulations governing the disclosure of such information, including, but not limited to, 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 State of [insert State] 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 State of [insert State] 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 State of [insert State] 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 State no longer has the legal authority or resources necessary to effectively carry out all aspects of this MOU, the State will notify FDA.

V. NAME AND ADDRESS OF PARTICIPATING AGENCIES

U.S. Food and Drug Administration
Center of 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
E-mail: StateMOU@fda.hhs.gov

[State]
TBD

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 30-day notice of termination. Notice of termination will be sent to the address listed in section V of this MOU.

b. If the State 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 30-days' notice of termination.

In case of termination, FDA will post a notice of the termination on its Web site and the State will notify all pharmacists, pharmacies, and physicians within the

State of the termination and advise them that as of 30 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 pharmacist, licensed pharmacy, or licensed 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 THE STATE OF [insert State]
By (Type Name)	By (Type Name)
Title	Title
Date	Date

Appendix A. Definition of Terms Used in the 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:** *Distribution* means that a compounded human drug product has left the facility in which the drug was compounded. Distribution includes delivery or shipment to a physician's office, hospital, or other health care setting for administration and dispensing to an agent of a patient or to a patient for the patient's own use.

  Note: 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 will not alter this condition.

- **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 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).