DRAFT 12/23/98

MEMORANDUM OF UNDERSTANDING ON INTERSTATE DISTRIBUTION OF COMPOUNDED DRUG PRODUCTS BETWEEN THE [STATE AGENCY] AND THE U.S. FOOD AND DRUG ADMINISTRATION

I. PURPOSE

This Memorandum of Understanding (MOU) establishes a cooperative program between the [State agency] and the U.S. Food and Drug Administration (FDA) regarding the regulation of interstate distribution of compounded drug products in accordance with section 503A of the Federal Food, Drug, and Cosmetic Act (FFDCA), 21 U.S.C. 353a.

II. BACKGROUND

A. On November 21, 1997, President Clinton signed into law the Food and Drug Administration Modernization Act of 1997 (Modernization Act). Section 127 of the Modernization Act, entitled "Application of Federal Law to Practice of Pharmacy Compounding," amended the FFDCA by adding a new section 503A governing the practice of pharmacy compounding, to become effective one year after enactment.

B. Section 503A(a) exempts a drug product from certain provisions of the FFDCA provided that the drug product meets the requirements of, and is compounded in accordance with, section 503A. Section 503A(a) specifies that a drug product may not be deemed adulterated under section 501(a)(2)(B), misbranded under section 502(f)(1), or an unapproved new drug under section 505 if the drug product "is compounded for an identified individual patient based on the unsolicited receipt of a valid prescription order or a notation, approved by the prescribing practitioner, on the prescription order that a compounded product is necessary for the identified patient, if the drug product meets the requirements of this section" and the compounding is performed as follows:

1. By a licensed pharmacist in a State-licensed pharmacy or Federal facility or by a licensed physician on a prescription order for an individual patient made by a licensed physician or other licensed practitioner authorized by State law to prescribe drugs; or

2. By a licensed pharmacist or licensed physician in limited quantities before the receipt of a valid

prescription order for an individual patient and is based on a history of the licensed pharmacist or licensed physician receiving valid prescription orders for compounding the drug product that have been generated solely within an established relationship between the licensed pharmacist/physician and (a) the individual patient for whom the prescription order is provided or (b) the physician or other licensed practitioner who writes the prescription order.

C. Section 503A(b)(3)(B) establishes that to qualify for the exemptions in section 503A, the drug product must be compounded in accordance with either of the following:

1. It is compounded in a State that has entered into a memorandum of understanding with FDA that addresses the interstate distribution of inordinate amounts of compounded drug products and provides for investigation by a State agency of complaints related to compounded drug products distributed outside such State; or

2. It is compounded in a State that has not entered into such an MOU but the licensed pharmacist, pharmacy, or

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.

D. Section 503A(b)(3) directs FDA, in consultation with the National Association of Boards of Pharmacy (NABP), to develop a standard MOU for use by States in complying with these provisions concerning the interstate distribution of compounded drug products. In developing this standard MOU, FDA and the NABP recognized that it is important that Federal and State officials cooperate, communicate, and share information regarding pharmacies and compounding. The standard MOU also reflects FDA's policy to defer to State and local officials for the regulation of the day-to-day practice of pharmacy, to the extent permitted under the FFDCA.

III. SUBSTANCE OF AGREEMENT

A. This MOU sets forth the responsibilities of the [State agency] and FDA regarding the following matters involving

the interstate distribution of compounded drug products: (1) investigation of and response to complaints relating to compounded drug products distributed outside of [State] and (2) response to the distribution of inordinate amounts of compounded drug products in interstate commerce. By signing this MOU, the [State agency] affirms that it now possesses and shall 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.

B. Complaints About Compounded Drugs

1. The [State agency] has primary responsibility for collecting complaint information and investigating complaints associated with the use of drug products compounded by a pharmacist, pharmacy, or physician located in [State]. Primary responsibility for investigating complaints involving pharmacy-compounded drug products will generally lie with the [State Board of Pharmacy] and similar responsibility for physician-compounded drug products will generally lie with the [State Medical Licensing Board], except where State

laws otherwise require. The [State Board of Pharmacy] and [State Medical Licensing Board] should cooperate in investigating any complaints involving overlapping jurisdiction.

2. Complaints to be investigated include, but are not limited to, reports of serious adverse drug experiences and alleged violations of the FFDCA, including, but not limited to, (1) compounding that may not qualify for the exemptions in section 503A and (2) compounding of a drug product that is in violation of Section 501(b) or (c) of the FFDCA, i.e., the drug product's strength differs from, or its purity or quality falls below, the standards in an official compendium (or, for a noncompendial drug, the strength, purity, or quality that the product purports or is represented to possess). A serious adverse drug experience is defined, for purposes of this MOU, as an experience that results in death, immediate risk of death, inpatient hospitalization or prolongation of existing hospitalization, a persistent or significant disability or incapacity, or a congenital anomaly or birth defect, or an experience that may jeopardize the patient and

require medical intervention to prevent one of the outcomes listed above.

3. The compounding of a drug product (or products) that meets any of the following criteria fails to qualify for the exemptions in section 503A of the FFDCA and, therefore, may be in violation of one or more provisions of the FFDCA:

   a. It is not compounded for an identified individual patient based on the unsolicited receipt of a valid prescription order or a notation, approved by the prescribing practitioner, on the prescription order that a compounded product is necessary for the identified patient.

   b. It appears on a list of drug products published in an FDA regulation that have been withdrawn or removed from the market because they have been found to be unsafe or not effective.

   c. It has been identified in an FDA regulation as presenting demonstrable difficulties for

compounding that reasonably demonstrate an adverse effect on its safety or effectiveness.

d. It has been prepared using a bulk drug substance that was not manufactured by an establishment registered with FDA or is not accompanied by a valid certificate of analysis.

e. It has been prepared using a bulk drug substance that does not comply with a United States Pharmacopeia (USP) or National Formulary monograph and the USP Chapter on Pharmacy Compounding; or, if such a monograph does not exist, it is prepared using a bulk drug substance that is not a component of a drug approved by FDA; or if such a monograph does not exist and the bulk drug substance is not a component of a drug approved by FDA, the bulk drug substance does not appear on a list of such substances published in an FDA regulation.

f. It has been improperly advertised or promoted contrary to section 503A(c) of the FFDCA. [Stayed

pending ongoing judicial proceedings]

g. It is essentially a copy of a commercially available drug product and has been compounded on a regular basis or in inordinate amounts contrary to section 503A(b)(1)(D) of the FFDCA.

h. It has been distributed interstate in inordinate amounts (either individually or along with other drug products), as described below in Section III.C, contrary to section 503A(b)(3)(B)(i) of the FFDCA.

4. By statute and/or regulation, the [State agency] agrees to investigate complaints in accordance with the following:

a. The [State agency] agrees to investigate complaints regarding drug products compounded by a pharmacist, pharmacy, or physician located in [State] that are shipped interstate. Such investigation should include communication in accordance with any applicable State statutes,

regulations, and administrative procedures with officials in the State(s) into which the compounded product was distributed and with the individuals reporting the complaint or the patients themselves.

b. Although the State in which the compounding pharmacy or physician is located will have primary responsibility for collecting complaint information and investigating a complaint, either that State or the State into which the subject product was distributed may propose to refer a regulatory or disciplinary matter to the other when it appears resolution can best be achieved under the authority of that other State.

c. Investigation of complaints by the [State agency] will include use of available laboratory services, where necessary, or, if it would facilitate the investigation, agreement to use another State’s laboratory services. FDA's laboratories will also be available to assist the States when necessary and feasible.

d. Based on the findings from the investigation, the State(s) having jurisdiction over the compounding pharmacist, pharmacy, or physician will take regulatory action in accordance with State statutes, regulations, and administrative procedures and/or ensure that corrective action is taken by the compounding pharmacist, pharmacy, or physician.

e. The [State agency] agrees to maintain records for at least three years on complaints, on investigations of complaints, and on any replies to complainants.

f. In the event of a significant dispute between two or more States about the handling of a complaint investigation, any State may request the assistance of the District Director of the appropriate FDA district office (District Director). The District Director will attempt to resolve the dispute so that the investigation of the complaint can proceed. The appropriate FDA district office is the closest district office to

the relevant compounding pharmacist, pharmacy, or physician.

C. Distribution of Inordinate Amounts of Compounded Drugs

1. The [State agency] agrees to take action regarding any pharmacist, pharmacy, or physician within its jurisdiction who distributes inordinate amounts of compounded drugs interstate. Such action may include State regulatory action, referral to FDA for action, or joint State-FDA action. For the purposes of this MOU, interstate distribution of an inordinate amount of compounded drugs occurs under either of the following circumstances:

   a. The number of compounded prescriptions dispensed or distributed interstate annually by a pharmacy or physician is equal to or greater than 20% of the total number of prescriptions dispensed or distributed (including both intrastate and interstate) by such pharmacy or physician; or

   b. The number of compounded prescriptions dispensed

or distributed interstate annually by a pharmacy or physician is less than 20% of the total number of prescriptions dispensed or distributed (including both intrastate and interstate) by such pharmacy or physician, but prescriptions for one or more individual compounded drug products (including various strengths of the same active ingredient) dispensed or distributed interstate constitute more than 5% of the total number of prescriptions dispensed or distributed.

2. The following are excluded from calculations to determine the number of compounded prescriptions dispensed or distributed interstate annually by a pharmacy or physician under Section III.C.1.a and b:

   a. Compounded drug products distributed interstate but “locally.” Such “local” interstate distribution is limited to distribution by a pharmacy or compounding physician to patients located within 50 miles of the pharmacy or compounding physician’s office, notwithstanding that such patients may reside in another State.

b. Compounded drug products distributed interstate that are compounded in response to a public health emergency or catastrophic situation (such as a flood, hurricane, or earthquake) that creates a need for additional supplies of compounded drug products to provide emergency care.

D. Meetings and Exchange of Information

1. At the end of the first year after signing the MOU, and at least every two years thereafter, FDA and the [State agency] will jointly review [State's] complaint investigation activities and responses to interstate distribution of inordinate amounts of compounded drugs to ensure that the terms of the MOU have been met.

2. The [State agency] and the District Director agree to meet periodically to discuss the established complaint handling procedures and actions to curtail interstate distribution of inordinate amounts of compounded drugs to ensure that they are adequate to protect the public and meet statutory requirements. The [State agency] and FDA will modify such procedures when determined to

be necessary by both parties.

3. The [State agency] agrees to forward to the District Director information on any significant violation of section 503A of the FFDCA (including significant violations that do not qualify for the exemptions in section 503A of the FFDCA, as described in Section III.B.3 above), violations of section 501(b) or (c) of the FFDCA, reported deaths, serious illnesses, and potential serious health hazards related to the interstate distribution of a drug product compounded in [State]. After appropriate investigation of such incidents by the [State agency] (independently or in conjunction with another State), the State or State(s) may either obtain corrective action through voluntary efforts on the part of the pharmacy or physician compounder or through regulatory sanctions imposed by the State(s), or refer the matter to the attention of the District Director for appropriate action.

4. The [State agency] and FDA may conduct a joint inspection of a pharmacy or physician’s office if requested by either party to investigate a complaint.

The parties agree to share any evidence obtained from such an inspection in accordance with applicable Federal and State laws.

5. FDA and the [State agency] agree to provide each other, upon request and in accordance with Federal and State law, information that each obtains on complaints about drug compounding in [State] and on the distribution of inordinate amounts of compounded drugs into or out of [State], as well as records that each maintains on inspections of compounders, complaint investigations, and actions to curtail interstate distribution of inordinate amounts of compounded drugs.

E. FDA Enforcement Authority and Legal Status of Agreement

The parties to this MOU recognize that FDA and the [State agency] retain all appropriate statutory and regulatory authority set forth in the FFDCA and attendant regulations and in State statutes and regulations, respectively. The parties also recognize that this agreement does not restrict either FDA or the [State agency] from taking appropriate enforcement action where necessary to ensure compliance with the FFDCA and attendant FDA

regulations or State statutes and regulations. This MOU does not create or confer any rights for or on any person.

IV. PERIOD OF AGREEMENT

When accepted by both parties, this MOU will be effective from the date of the last signature. This MOU will remain in effect unless it is terminated in writing by either party.

VI. APPROVAL

Approved and Accepted For The U.S. Food and Drug Administration	Approved and Accepted For The State of _____
By: _____	By: _____
Title: Associate Commissioner for Regulatory Affairs	Title: _____
Date:	Date: