National Home Infusion Association
Providing solutions for the infusion therapy community

January 30, 2014

Margaret A. Hamburg, M.D.
Commissioner of Food and Drugs
Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane
Room 1061
Rockville, Maryland 20852

Re: Draft Guidance "Pharmacy Compounding of Human Drug Products Under Section 503A of the Federal Food, Drug, and Cosmetic Act" (Docket Number: FDA–2013-D–1444)

Dear Commissioner Hamburg:

The National Home Infusion Association (NHIA) submits these comments on the draft guidance made available on December 4, 2013 by the Food and Drug Administration (FDA) entitled "Pharmacy Compounding of Human Drug Products Under Section 503A of the Federal Food, Drug and Cosmetic Act." NHIA is a national membership association for clinicians, managers and organizations providing infusion therapy services for patients in the home and outpatient settings.

We have focused our comments on the establishing, maintaining and updating of lists of (1) drug products that may not be compounded because they have been withdrawn or removed from the market because the drug product or its components have been found to be unsafe or not effective (Withdrawn or Removed List); (2) bulk drug substances that should be able to be used to compound drug products in accordance with section 503A (Bulk Drug Substances List); and (3) the drug products that present demonstrable difficulties for compounding (Difficult-to-Compound List). In addition, NHIA previously submitted the attached comments on the Memorandum of Understanding (MOU) between FDA and the States, which the FDA plans to issue in accordance with Section 503A(b)(3)(B) of the Federal Food, Drug and Cosmetic Act.

Before discussing the establishing, maintaining and updating of the lists noted above, NHIA would like to comment further on the Standard MOU that the FDA will be developing in consultation with the National Association of Boards of Pharmacy (NABP). NHIA suggests that, if a state determines that a pharmacy is acting as a 503A facility and that the pharmacy is otherwise compliant with all applicable state laws, the FDA should not mandate particular state actions that are based solely on the percentage of product that crosses the state border. Rather, the state should have discretion in

determining the regulatory measures necessary to ensure the quality and safety of drug being shipped outside the state. NHIA also suggests that, before publishing for comment any MOU that defines "inordinate quantities" of out of state shipments, the FDA conduct a study as to what should constitute "inordinate quantities" of drug product in today's market. As NHIA noted in our previous correspondence, the legislative history of section 503A clearly indicates that "'inordinate' quantities means amounts typically associated with ordinary commercial drug manufacturing (emphasis added)."[1] NHIA believes that the MOU should reflect an understanding of current pharmacy practices as well as commercial drug manufacturers' practices, and should not simply impose an arbitrary ceiling on states, pharmacies, and out-of-state purchasers that is based on perceptions from the late 1990s.

NHIA understands that FDA is obligated by Section 503A to develop a Withdrawn or Removed List, a Bulk Drug Substances List, and a Difficult-to-Compound List. In carrying out these obligations the FDA should utilize a transparent and open process that provides stakeholders with meaningful opportunity to comment on the products that the FDA proposes to include on these lists.

Specifically, NHIA recommends that the FDA utilize a formal notice and comment period not only for establishing these lists, but also for updating them. NHIA intends to submit separate comments in response to the notices issued by the FDA regarding the Bulk Drug Substances List and the Difficult-to-Compound List. NHIA recommends that the FDA also establish a new, updated Withdrawn or Removed List. FDA has not updated the current Withdrawn or Removed List since it was originally drafted in 1999. There have been significant developments in pharmacy practice and the pharmaceutical industry over the past 15 years, and as a result, the existing list is antiquated. NHIA believes that the FDA should issue a notice requesting nominations for drugs that should be included on the Withdrawn or Removed List or excluded from the list.

In addition, we believe that the FDA should conduct public meetings related to the lists for interested stakeholders to discuss which drug products should initially be included on the various lists. FDA also should meet with provider groups and trade associations to discuss the drug products being considered for the lists. We believe that soliciting feedback through several channels is important to ensure that the FDA obtains the most helpful and current advice about the appropriate drug products to be included on these lists. After the FDA receives feedback through these channels, NHIA recommends that the FDA issue each list in proposed form so that stakeholders have the opportunity to comment on the drug products included therein.

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[1] U.S. Senate. Committee on Labor and Human Resources. *Food and Drug Administration Modernization and Accountability Act of 1997: Report Together with Minority Views (to accompany S. 830)* (S.Rpt. 105-43). Washington: Government Printing Office, 1997, p. 68.

In addition, the FDA should regularly update each of the three lists, by an open process that provides stakeholders with meaningful opportunities to provide comments. The FDA may consider establishing a regular schedule under which the Agency requests nominations for products that should be added to or removed from each of the three lists, considers the feedback received, and updates the lists accordingly. This predictable and transparent process will encourage stakeholders to continuously invest time in preparing and submitting thoughtful, evidence-based recommendations of the drug products that the FDA should consider adding to or removing from the lists.

Also, due to the unique needs of each individual patient and the lag between scientific developments and regulatory updates, NHIA believes that the FDA should establish a process for physicians and pharmacists to petition to have a drug made available for compounding even if it is on the Withdrawn or Removed List or the Difficult-to-Compound List. Should a drug shortage occur where a drug is needed that is on these lists it may become imperative that a process be in place to move swiftly to make the drug available for compounding.

Finally, NHIA recognizes that the FDA has important responsibilities to enforce section 503A and its associated regulations. However, Section 503A also reflects Congress' recognition of the states' important role in regulating compounded drug products. Many states allow for pharmacy technicians to compound under the supervision of a pharmacist, and in those states the FDA should allow pharmacies under Section 503A to employ and utilize individuals that compound under the supervision of a practitioner licensed to compound under state law. This would adequately recognize the flexibility afforded by some state laws and provide for variability between states on how pharmacy technicians are regulated and licensed. We encourage FDA to remain mindful of the states' licensure and regulatory responsibilities in this regard.

Please feel free to have your staff contact Kendall Van Pool, NHIA Vice President of Legislative Affairs, at (703) 838-2664 or kendallvanpool@nhia.org should you want to discuss our comments further. Thank you for your consideration of NHIA's comments.

Sincerely,

Russell Bodoff
President & CEO
National Home Infusion Association

Attached: NHIA Memorandum of Understanding Comments

NHIA
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January 6, 2014

Margaret A. Hamburg, M.D.
Commissioner of Food and Drugs
Division of Dockets Management (HFA-305)
Food and Drug Administration
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Rockville, Maryland 20852

Re: Draft Guidance "Pharmacy Compounding of Human Drug Products Under Section 503A of the Federal Food, Drug, and Cosmetic Act"

Docket Number: FDA–2013-D–1444

Dear Commissioner Hamburg:

The National Home Infusion Association (NHIA) submits these comments on the draft guidance entitled "Pharmacy Compounding of Human Drug Products Under Section 503A of the Federal Food, Drug and Cosmetic Act" made available on December 4, 2013 by the Food & Drug Administration. NHIA is a national membership association for clinicians, managers and organizations providing infusion therapy services for patients in the home and outpatient settings.

This comment letter is limited to the FDA's planned issuance of a new standard Memorandum of Understanding (MOU) in accordance with Section 503A(b)(3) of the Federal Food, Drug, and Cosmetic Act (FD&C Act). NHIA will be submitting additional comments on other aspects of the draft guidance in a separate letter. We urge the FDA and the National Association of Boards of Pharmacy (NABP) to consider the unique nature of home infusion therapy and the well-established track record of home infusion pharmacies when developing the revised standard MOU.

Background on Home Infusion Therapy

Infusion therapy involves the administration of medication through a needle or catheter. The drug is generally administered intravenously, although it also may be provided through other non-oral routes such as via an intramuscular injection or epidural. Infusion therapy is indicated for patients with medical conditions that cannot be treated effectively with oral medications, such as patients diagnosed with infections that are unresponsive to oral antibiotics; cancer and cancer-related pain; and congestive heart failure.

Nonetheless, the FDA previously released a draft MOU on December 23, 1998 that specified that interstate distribution of an "inordinate amount of compounded drugs" occurs if the number of compounded prescriptions distributed interstate on an annual basis is equal to or greater than 20 percent of the total number of prescriptions dispensed or distributed by that pharmacy (including both intrastate and interstate prescriptions), or if prescriptions for one or more individual compounded drug products (including varying strengths of the same active ingredient) constitute more than 5 percent of the total number of prescriptions dispensed or distributed by the pharmacy.

We do not know the basis for these thresholds, but they appear to be arbitrary and inconsistent with Congress' intent that the "inordinate" language be limited to activities that are associated with manufacturing. More relevant to home infusion, however, we have two additional objections to this approach. The preparation and dispensing of an infusion drug subject to a patient-specific prescription is not an element of common manufacturing, regardless of whether the drug is delivered across a state border. In addition, the dispensing of an infusion drug to a specific patient is not a "distribution" of the drug, and thus is not a proper subject of the MOU.

NHIA encourages the FDA and the NABP to refrain from imposing such an arbitrary cap on the interstate dispensing of compounded drug products when drafting the new standard MOU. This type of limitation would not reflect advances in technology, current shipping techniques, quality controls and current practices by home infusion providers since 1999.

The practice of pharmacy compounding has changed significantly since the original MOU language was proposed in 1998. The practice of sterile compounding by licensed pharmacies in the late 1990s was based on published recommendations that lacked regulatory enforcement—a practice that was fundamentally changed with the adoption of enforceable sterile compounding standards in Chapter <797> by the United States Pharmacopeia (USP) in 2004. Organizations such as the American Society of Health-System Pharmacists and USP had issued pharmacy compounding practice recommendations in the late 1990s that centered on the pharmacist's responsibility for ensuring proper preparation, labeling, storage, dispensing, and delivery of compounded sterile products. While the published recommendations addressed many of the concerns of the profession, formal accountability to regulatory agencies for compliance with these recommendations was lacking.

Efforts to remedy the enforcement of sterile compounding standards continued, and culminated on January 1, 2004, when the first official and enforceable sterile preparation compounding standard in the United States was published as USP Chapter <797>. The expert committee responsible for writing USP Chapter <797> received considerable feedback and comments after the chapter was published. Based on many of these comments, the committee proposed revisions to USP Chapter <797> in the *Pharmacopeial Forum* 32(3), May–June 2006. The revision process included a call for public comments on the proposed revisions, and the response was overwhelming with

MOU Implementation

The FDA noted in the guidance that it does not intend to enforce the 5% limit on interstate distribution until 90 days after the FDA has finalized the MOU and made it available to the States for their consideration and signature. NHIA has concerns with this limited window for States to consider and negotiate with the FDA on provisions within their MOU. Each State may have specific needs that differ from other States, and the FDA should be prepared to be flexible and work with states to resolve State specific matters.

States and their Boards of Pharmacy all have different oversight structures, and in some cases States may be required by their own sunshine laws to take longer than 90 days to sign the MOU. Also, it is quite possible that some Boards of Pharmacy may lack the authority to sign the MOU. This issue was apparent during the comment period on the 1998 MOU. The Alaska Board of Pharmacy commented that "the board has determined that they do not have the authority to comply with the Memorandum of Understanding as presently written." Several other States submitted their own draft memorandums for consideration with the FDA. The FDA should be responsive to the needs of the States and should reconsider a hard 90 day enforcement timeline for the 5% limit on interstate distribution.

We look forward to working with the FDA and NABP in a collaborative way to ensure the MOU is drafted to encourage coordination between state boards and FDA. Please feel free to have your staff contact Kendall Van Pool, NHIA Vice President of Legislative Affairs, at (703) 838-2664 or kendallvanpool@nhia.org should you want to discuss our comments further. Thank you for your consideration of this NHIA's comments.

Sincerely,

Russell Bodoff

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President & CEO
National Home Infusion Association

CC: The National Association of Boards of Pharmacy