March 20, 2013

The Honorable Tom Harkin
Senate Committee on Health, Education, Labor and Pensions
731 Hart Senate Office Building
Washington, DC 20510

The Honorable Lamar Alexander
Senate Committee on Health, Education, Labor and Pensions
455 Dirksen Senate Office Building
Washington, DC 20510

Dear Chairman Harkin and Ranking Member Alexander:

On behalf of the International Academy of Compounding Pharmacists (IACP), I am writing to provide comments and insights into a conceptual model proposed by the Food and Drug Administration (FDA) that is intended to address the safety of compounded medications and clarify the FDA's authority in this area.

The IACP appreciates the opportunity to work with the Senate Health, Education, Labor, and Pensions (HELP) Committee to ensure that a tragedy like the one that occurred last year, when compounded preparations dispensed by a Massachusetts licensed pharmacy caused an outbreak of fungal meningitis, never happens again.

The IACP is a non-profit professional association representing more than 2,700 pharmacists, technicians, students, and members of the compounding community who focus on the specialty practice of pharmacy compounding. The IACP is and has been committed to working in collaboration with state and federal officials to ensure the safe practice of pharmacy compounding. In December 2012, the Academy issued a series of recommended changes *(see attachment)* to state pharmacy laws and regulations that it believes will both enhance the protection of public health while preserving the professional decision making of pharmacists in the selection and preparation of customized medication solutions. These proposed changes address three key areas: inspection authority and adequate funding of all state Boards of Pharmacy; compliance with laws and regulations by all pharmacists and pharmacy technicians in all practice settings, as well as other health care practitioners involved in compounding; and adherence to nationally recognized quality standards.

We ask the Committee to keep in mind that a significant number of people have unique health needs that off-the-shelf, one-size-fits-all prescription medicines cannot meet. These include children, the elderly, and those for whom manufactured drug products are not available in the appropriate strength, dosage form, or composition. For them, customized medications are the only way to better health and those valuable preparations are available only by compounding.

Any recommendation or proposal must be considered and balanced in a manner that does not restrict a doctor's ability to prescribe and obtain compounded medications for those patients who require them as part of their necessary therapy. Moreover, manufacturers often discontinue a number of FDA-approved drugs that serve a limited population. In many of these cases, the only option left for doctors and their patients is to have a compounding pharmacist make the discontinued drug pharmaceutical grade ingredients obtained from an FDA-registered supplier.

While the IACP strongly believes that the regulation of compounding should continue to be overseen by state Boards of Pharmacy and that improvements may need to be made to current state pharmacy laws, we understand the importance in determining what greater clarity in differentiating between drug compounding and drug manufacturing may be needed. To that end, it is our understanding that the FDA has put forward a conceptual framework that would apply a "three pronged" test to determine when the activities of a compounding pharmacy should be subject to FDA oversight and jurisdiction rather than the state regulatory authorities, the Boards of Pharmacy. It is this proposal that the IACP has been asked to review and provide comment.

It is important to note that the following remarks and observations should not be construed as communicating either the IACP's support or opposition to the proposal, given the fact that we have not been provided with any written materials beyond the very general framework that was outlined in the FDA's testimony to the committee on November 15, 2012. In the event that a more formal proposal is released by the Committee or FDA, the IACP would welcome the opportunity to officially comment on such a plan.

Additionally, we have been asked to comment on a proposal that would list in statute certain products that FDA believes are not appropriate for compounding under any circumstances.

Based on FDA's testimony and other public statements, we understand that the FDA's proposal is as follows:

The FDA Conceptual Framework As Understood by IACP

There would be a three-part test used to determine whether or not an entity is engaged in traditional drug compounding:

1. *Is the compounded product a sterile preparation?*
2. *Is the compounded product being shipped across state lines?*
3. *Is the compounded product being prepared prior to the receipt of a prescription or order for a particular patient?*

If the answer to all three questions is "yes," then these products would fall under a new category of product overseen by FDA. Based on FDA's testimony before the Senate HELP Committee, FDA will likely categorize such products as "non-traditional compounding," rather than as a new tier of drug manufacturing.

For such products:

1. *No pre-market approval requirements would be required.*
2. *No adverse event reporting would be required.*
3. *Current good manufacturing practices (cGMPs) would be required. It is unclear whether FDA would develop any alternative standards.*

Hospital system pharmacies engaged in sterile compounding would be exempted from these requirements, even if they satisfy all three prongs of the aforementioned test. Also test would not apply to non-sterile compounding.

According to FDA's testimony, it is possible that FDA may also seek the following authorities with respect to this new category of products:

- *The authority to collect and test samples of such compounded drugs and to examine and collect records belonging to that compounding pharmacy, including records of prescriptions received, products shipped, volume of operations, and operational records such as batch records, product quality test results, and stability testing results.*
- *A label identifying the nature and source of the compounded product.*
- *Require pharmacies compounding such products to register with FDA.*

At the outset, the IACP would like to reiterate its position that the authority to determine when a pharmacy or pharmacist exceeds their scope of practice should and must remain exclusively with the state Boards of Pharmacy. State Boards of Pharmacy, through their ongoing regular inspections, knowledge of unique state laws, regulations and rules, as well as having practicing pharmacists as their members who are engaged in day-to-day patient care, are in the best possible position to determine whether a pharmacy has exceeded its scope of practice or engaged in activities that may constitute manufacturing. That said, the IACP recognizes that the oversight and regulation of prescription drug manufacturing rests with FDA, and that the Agency has the authority to identify and require the registration of any entities it believes are engaged in such activity.

On this point, IACP believes that the FDA proposal should include a key component, which is either missing or omitted from the current conceptual "three pronged" test – that is the requirement that the Agency coordinate any and all of its actions and communications with state Boards of Pharmacy whenever the Agency has concerns regarding an individual pharmacy's activities or practices. Efficient and effective communication with state Boards of Pharmacy is essential to prevent the Agency's unilateral determination that a pharmacy's professional and business activities exceed the state specified scope of practice. Without such coordination any proposal is unlikely to achieve its goal or to improve public health safety.

We urge the Committee to consider requiring that the FDA coordinate any and all of its pharmacy related actions – including on-site inspections – with the appropriate state Board of Pharmacy.

Much discussion has surrounded the point at which a compounding pharmacy's dispensing of medications in some manner transitions from pharmacy practice into manufacturing. The proposed series of "tests" presented by the FDA are intended to define that transition point.

Unfortunately, the approach put forward by the FDA does not achieve this goal. Rather than determining when the scope and nature of pharmacy activity would raise the kinds of concerns associated with manufacturing, the proposal would take the unprecedented step of taking a category of compounding that is now regulated by the states and place it within the exclusive jurisdiction of FDA.

Traditional vs. Non-Traditional Compounding

Comments: As an initial matter, the IACP believes that any proposal advanced by the Committee should provide greater certainty on these issues rather than promote new, previously undefined concepts that have never been applied to either the practice of pharmacy compounding or drug manufacturing. For this reason, the IACP strongly opposes the use of the terms "traditional compounding" and "non-traditional compounding." Those terms are not defined in any professional or scientific literature nor are they recognized within pharmacy practice. Such a distinction will only serve to increase confusion and provide even less clarity to the issue of when the activities of a compounding pharmacy crosses the threshold into drug manufacturing.

Recommendation: Rather than create a new category of "drug compounding" oversight, as the proposal appears to do, IACP believes that whatever "tests" are used, if any, should instead be used to address the FDA's uncertainty over what constitutes manufacturing. Since FDA is already empowered by Congress to govern the manufacture of drugs, FDA has the existing authority to apply drug manufacturing regulations as they see fit within the law. The Academy believes that giving expanded FDA authority in a totally new area is premature, especially when the Agency still has not fully explained why it failed to follow-up with its own warning letters and inspections of New England Compounding Center.

This approach allows FDA to maintain its clear line of authority over drug manufacturing, while at the same time provide clearer guidance to pharmacies and pharmacists on when their activities may exceed their scope of practice. Just as important, it allows both the Committee and FDA to achieve its goal of additional clarity without having to expand the Agency's authority over the state regulated practice of pharmacy.

Is the Compounded Product a Sterile Preparation?

Comments: The IACP observes that the first "test" of the FDA proposal is limited to only sterile compounded preparations. We understand that sterile medications present a potentially greater health risk to patients, particularly if they are not prepared in accordance with United States Pharmacopeia (USP) Chapter <797> compounding guidelines. However, we wish to further understand the FDA's thinking and public safety concerns on this point. Specifically, the Academy is concerned that the Agency may intend to further expand authority to include non-sterile compounded preparations at some future date as well.

Is the Compounded Product Being Shipped Across State Lines?

Comments: The IACP observes that the second "test" of the FDA proposal, interstate shipment, could have significant unintended consequences on public health. States currently have the authority to decide when licensure of a non-resident pharmacy is appropriate and consistent with their laws and regulations. The interstate shipment of prescription drugs, irrespective of whether they are manufactured or compounded, is a critical, necessary and appropriate component of healthcare. The dispensing of a medication upon the existence of a prescriber-generated prescription or order, regardless of to whom it is dispensed or where it is shipped, is a function of normal pharmacy practice. The mere fact that a pharmacy may be shipping product over state lines is not a relevant indicator of manufacturing activity. Any test that looks at interstate shipping should take into consideration whether such shipments were in full compliance with state laws defining valid prescription orders and the involvement of an authorized prescriber.

Recommendation: The IACP respectfully suggests that a more effective "test" is whether a state Board of Pharmacy has made a determination that the pharmacy is engaged in activities outside of their scope of practice. If after an inspection, hearings, and appropriate due process as provided for within individual state laws, the state Board is in the best possible position to decide whether a pharmacy is engaged in manufacturing – regardless of whether that pharmacy is shipping medications in inter- or intra-state commerce.

Is the Compounded Product Being Prepared for a Specific Patient?

Comments: The IACP is especially concerned with the FDA's third "test" and its statement that a pharmacy may not prepare a compounded medication prior to the receipt of a valid prescription or medical order. As proposed, such a position would essentially eliminate the preparation of compounded medications commonly referred to as "anticipatory compounding." Anticipatory compounding is the preparation of compounded medications based upon historical prescriptions received by the pharmacy and is in no way associated with manufacturing activities. Anticipatory compounding is a form of inventory management, which enables the pharmacy and pharmacist to prepare compounded preparations in amounts sufficient to meet the needs of patients and prescribers and is recognized both within the profession and in state law. It is not a determination of whether a pharmacy is engaged in manufacturing-like activities.

The Academy also believes that the FDA's third "test" contradicts and effectively eliminates existing state authority that permits authorized prescribers from issuing prescriptions or medical orders for medications for their "office-use." By specifically requiring only patient-specific prescriptions as part of the "test", the FDA appears to circumvent those individual state's laws, regulations and rules that enable prescribers to obtain compounded preparations for administration to or treatment of patients within their practices. Office-use dispensing is the preparation, labeling, and dispensing of a medication by a pharmacist and pharmacy upon the receipt of a prescription or medical order from an identified authorized prescriber (e.g. physician, nurse practitioner, dentist, veterinarian, etc.) for that prescriber's use in the treatment of or administration to a patient during their normal course of medical practice. Office-use dispensing includes both manufactured prescription drug products and compounded preparations. Many states currently have provisions permitting office-use dispensing and other states are actively reviewing, clarifying, and issuing regulations on this very issue. Under the FDA concept, those appropriate state actions would essentially be nullified.

Recommendation: The mere act of preparing a compounded medication prior to the receipt of a valid prescription or medical order issued by an authorized prescriber incorrectly places the focus on the preparation, rather than on the dispensing, shipment or distribution of a compounded medication. The true test should be whether or not a pharmacy has distributed a prescription medication in the absence of such a prescriber directive as defined within state law. This is a much more appropriate test as it provides a potentially more accurate indicator of activities that may be deemed drug manufacturing.

FDA's Proposed Exemption for Hospitals or Other Health Care Facilities

Comments: The IACP strongly supports the application of any legislation or regulation pertaining to compounding to all pharmacy practices, whether they are free-standing or located within a hospital or health care facility. Exempting any practice site, such as hospitals, creates two distinctly different categories of patient safety protection. This is especially questionable in light of the volume and types of compounding done in hospital pharmacies, a substantial amount of which includes sterile compounded preparations.

Recommendation: We would urge the Committee to consider the implications of such an exemption on public safety and the perception of exempting any entity on the mere basis that it is located in a hospital or health care facility. While we understand that the application of any new rules and regulations may have to be modified to take into consideration other existing regulatory agencies and quality assurance agencies that oversee hospital safety and practices (i.e., the Joint Commission), such a challenge is manageable and should not outweigh the overall interest in ensuring patient safety.

Overall, we are concerned that the "three pronged test" proposed by FDA fails to provide any clarity in helping determine when a compounding pharmacy or pharmacist meets the state-regulated standard and when their actions have crossed into manufacturing that is subject to FDA oversight. Without such clarity we do not believe this proposal will help to protect patients and avoid similar tragedies in the future.

Additional FDA Concepts

According to FDA's testimony, it is possible that FDA may also seek the following authorities with respect to this new category of products:

- *The authority to collect and test samples of such compounded drugs and to examine and collect records belonging to that compounding pharmacy, including records of prescriptions received, products shipped, volume of operations, and operational records such as batch records, product quality test results, and stability testing results.*
- *A label identifying the nature and source of the compounded product.*
- *Establish a list of prescription medications which should not be compounded.*

Scope of FDA Inspection Authority

The IACP notes that the FDA currently has the authority to collect and test samples of compounded preparations upon the presentation of the Agency's Form 484 and in compliance with its established policies and procedures. This is not new authority and we question why this is even being raised.

The IACP notes that the FDA also has the ability to obtain access to records of prescriptions, products shipped, volume of operations, and other such documents through a court-affirmed process. Since 1962, under Section 704(a)(2)(A) of the Federal Food, Drug and Cosmetic Act (FFDCA), a pharmacy may claim an exemption from the FDA's broad inspectional authority under certain circumstances:

> *Pharmacies which maintain establishments in conformance with any applicable local laws regulating the practice of pharmacy and medicine and which are regularly engaged in dispensing prescription drugs or devices, upon prescriptions of practitioners licensed to administer such drugs or devices to patients under the care of such practitioners in the course of their professional practice, and which do not, either through a subsidiary or otherwise, manufacture, prepare, propagate, compound, or process drugs or devices for sale other than in the regular course of their business of dispensing or selling drugs or devices at retail.*

In the event that a pharmacy exercises its right to claim the FFDCA exemption, the Agency is empowered to obtain a court order, warrant, or subpoena to obtain those records, if it deems such action necessary.

The IACP has seen no evidence that the FDA has been unable to obtain access to the records they seek under the existing process. The Agency has provided no data on the number of pharmacies it has inspected, the number of pharmacies which did or did not claim the exemption, the number of court orders, warrants, or subpoenas that were requested to obtain those records after an exemption was claimed, or whether any of those court requests were declined.

Identifying Labels for Compounded Products

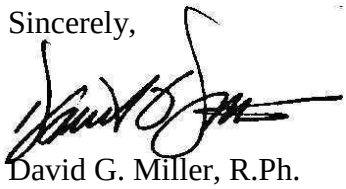
With respect to an identifying label, the IACP has a formal guideline for its members that requires all compounded preparations be labeled as such so that the prescriber and/or patient is readily aware that the medication has been compounded.

"Do Not Compound" List

The IACP continues to point out that the recommendation to create and maintain a "do not compound" list by the FDA based upon patient safety already exists under FFDCA Section 503A(d)(1). Such a list was created by the Agency and is continually promoted to the compounding profession by the IACP to educate its members and others. The Academy respectfully points out to the Committee that even given such authority under Section 503A(d)(1), the Agency has not updated the current "do not compound" list in more than ten years. In fact, several manufactured FDA-approved drug products have been withdrawn from the market for reasons of significant threat to patient safety; the Agency has never included those medications on the existing "do not compound" list. The IACP believes that any changes to this list must be done in an open, structured and, most importantly, timely manner that solicits and accepts the position and opinions of the medical and pharmacy community. The IACP also believes that if the collective professional community and the FDA determine that a product should not be compounded due to evidence of patient safety, it should also not be available from a manufacturer.

In closing, as the Committee seeks to craft legislation in this area, we would urge you to not lose sight of the fact that pharmacy compounding is vital to our health care system and to ensuring patient access to appropriate medications for a variety of medical conditions. We appreciate the opportunity to provide comments to the Committee and look forward to continuing our work with you on this important issue.

Sincerely,



David G. Miller, R.Ph.
Executive Vice President and CEO

Attachment: IACP

CC: Members, IACP Board of Directors