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ONE HUNDRED THIRTEENTH CONGRESS
Congress of the United States
House of Representatives

COMMITTEE ON ENERGY AND COMMERCE

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May 3, 2013

The Honorable Margaret A. Hamburg, M.D.
Commissioner
U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

Dear Commissioner Hamburg:

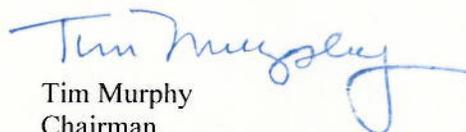
Thank you for appearing before the Subcommittee on Oversight and Investigations on Tuesday, April 16, 2013, to testify at the hearing entitled "A Continuing Investigation into the Fungal Meningitis Outbreak and Whether It Could Have Been Prevented."

Pursuant to the Rules of the Committee on Energy and Commerce, the hearing record remains open for ten business days to permit Members to submit additional questions for the record, which are attached. The format of your responses to these questions should be as follows: (1) the name of the Member whose question you are addressing, (2) the complete text of the question you are addressing in bold, and (3) your answer to that question in plain text.

To facilitate the printing of the hearing record, please respond to these questions and requests by the close of business on Friday, May 17, 2013. Your responses should be e-mailed to the Legislative Clerk in Word format at brittany.havens@mail.house.gov and mailed to Brittany Havens, Legislative Clerk, Committee on Energy and Commerce, 2125 Rayburn House Office Building, Washington, D.C. 20515.

Thank you again for your time and effort preparing and delivering testimony before the Subcommittee.

Sincerely,



Tim Murphy
Chairman
Subcommittee on Oversight and Investigations

cc: Diana DeGette, Ranking Member, Subcommittee on Oversight and Investigations

Attachment

Attachment—Additional Questions for the Record

The Honorable Tim Murphy

1. Please explain the new policy and process FDA has established to enhance communications with the State pharmacy boards.
2. Please explain what steps have been taken to ensure that Warning Letters and related correspondence are approved in a timelier manner.
3. Please explain what constitutes a “proactive inspection” versus a “for cause” inspection. Which official or employee at FDA made the decision to suspend “proactive” inspections of compounding operations and what was the threshold that needed to be crossed prior to FDA conducting such an inspection in 2011 and 2012?

The Honorable Michael C. Burgess

1. According to the recently released OIG report, *High-Risk Compounded Sterile Preparation and Outsourcing by Hospitals that Use Them*, 92% of hospitals produce sterile compounds and only about half had USP 797-compliant clean rooms. In addition, about one half of hospitals stated that cost and space will be major challenges to comply with 797. Furthermore, the report concludes that hospitals intend to increase the amount of sterile compounding they produce onsite in the wake of drug shortages. Therefore, will FDA include hospitals in the compounding framework that FDA is proposing?
2. The Committee is aware that FDA is currently inspecting pharmacies to GMP standards. How are you determining whether to inspect as a manufacturer versus a compounding pharmacy and when does this analysis take place? Are you partnering with and in discussions with State Board of Pharmacies to determine if the pharmacy has exceeded state licensing authorities?

The Honorable Pete Olson

1. Currently, we understand there is a mechanism for compounding pharmacies to register with the FDA. What authority does this give FDA over the pharmacies that voluntarily register with the FDA? What standards are enforced on these registered pharmacies?

The Honorable Morgan Griffith

1. If an establishment refuses to allow FDA inspectors to enter, please explain the process for obtaining a warrant. In the past 5 years, how many times has this occurred? Has a judge ever refused? On average, how long has it taken FDA to get a warrant since the date FDA inspectors initially attempted to enter the facility?

The Honorable Bill Johnson

1. For each Adverse Event Report FDA received associated with a product produced by NECC or Ameridose, please document what actions the agency took in response, including, but not limited to, whether FDA informed the Massachusetts Board of Pharmacy.
2. Please describe how Adverse Event Reports submitted to FDA's MedWatch system are shared with the correct FDA offices and employees.
3. In addition to the numerous Adverse Event reports FDA had received associated with Ameridose products harming patients, the agency received several alarming complaints from an employee at Ameridose, including the fact that there was mold growing in one of the sterile compounding rooms. Please explain what information FDA needed to receive about a company prior to conducting a "for cause" inspection during your tenure as Commissioner? What were the criteria used?

The Honorable Renee Ellmers

1. Please submit a list of all complaints relating to NECC or Ameridose that FDA forwarded or reported to the Massachusetts Board of Pharmacy.

The Honorable Edward J. Markey

1. I recently released a report entitled "State of Disarray" that analyzed state oversight of compounding pharmacies and was based on information provided directly from the state boards of pharmacy¹. This report found that only 2 states, Mississippi and Missouri, routinely track compounding pharmacies in their state. And none of the states have requirements that its board of pharmacy be notified on the quantity of compounded drugs produced or whether a pharmacy is shipping drugs over state lines. Given the lack of information maintained by the states, do you think that states can currently do an adequate job of overseeing interstate commerce engaged in by compounding pharmacies within the state? Please explain.
2. As you are aware, sterile compounding, particularly using non-sterile components, carries the greatest danger to public health. Yet, only a handful of states (13 states) know which pharmacies are providing sterile compounding services, and even fewer of these states (5 out of 13 states) have inspectors that are specifically trained for identifying problems with sterile

¹ <http://markey.house.gov/press-release/markey-report-compounding-pharmacies-going-untracked-unregulated-under-inspected-coast#overlay-context=>

compounding. The current system allows any state to come up with their own regulatory framework for sterile compounding, resulting in a patchwork of standards across the nation.

- a. Do you think that the FDA should impose a mandatory, enforceable and uniform standard for sterile compounding applied across all 50 states, to ensure consistency in the safe production of sterile drugs? Please explain.
 - b. Do you think FDA should play a role in ensuring that all sterile compounding pharmacies are held to this same standard and enforced against uniformly? Please explain.
3. A recurring theme that came up in the responses provided by the state boards of pharmacy was that when issues arise with out-of-state pharmacies, states do not consistently inform the state where the pharmacy is physically located or other states where the drugs were shipped. As a result states are unable to effectively police compounding pharmacy activities in other states because they are simply not aware of what occurs outside their borders. Do you think FDA should be responsible for policing the interstate commerce associated with all compounding pharmacies? Please explain.
4. The report indicated that states do not have a requirement that compounding pharmacies report the volume of drugs they are providing in advance of a prescription, or in response to prescriptions. Given this lack of information on the state level, it would be impossible for states to focus enforcement activities on facilities that are the largest producers of compounded drugs.
 - a. Would the FDA support the requirement that compounding pharmacies provide information on the volume of drugs to FDA or the states?
 - b. Would the FDA find it helpful to have this information, for purposes of determining which of these facilities may be manufacturing drugs and are therefore subject to the requirements of drug manufacturers?
5. The report also indicated that states generally do a poor job maintaining historical records. For example, only 64 percent of the boards of pharmacy that responded to the investigation were able to provide the number of pharmacies that were licensed in their state over the last decade. Furthermore, state licensing practices differ greatly; as some states compile community pharmacies with drug dispensers, distributors and wholesalers and others license these categories separately. Moreover, typically the states do not maintain pharmacy inspection records that enable easy searching and compiling of statistics and data, making it

impossible for many of the states to identify issues pertaining to safety, cleanliness, sterility and other issues that came to light in the New England Compounding Center tragedy. Do you think the current licensing and record keeping practices of the states would enable them to solely and effectively identify systemic and repeated compounding pharmacy safety problems?

The Honorable G. K. Butterfield

1. Will Sequestration impact the FDA's ability to inspect compounding facilities and adequately address complaints associated with compounded drugs? Will sequester increase the possibility that a contamination situation could occur again?
2. Does reassigning investigators who would normally be conducting inspections at conventional drug manufacturers divert resources from other areas including pharmaceutical approval?
3. In the risk-based framework recommended by the FDA, would the agency have the appropriate resources to test samples of compounded drugs and examine records of compounding pharmacies?
4. It is my understanding that there is a mechanism for compounding pharmacies to register with FDA. What authority does this give FDA over the pharmacies that voluntarily register with the FDA? What standards are enforced on these registered pharmacies?
5. What improvements in communication and oversight have been implemented by the Food and Drug Administration in response to meetings with State Pharmacy boards?
6. How are patients notified about recalls of compounded drugs they have been prescribed? Are patients made aware of symptoms of defective compounded drugs and treatment options if infected?
7. What additional legal framework would provide the FDA with the tools needed to identify and adequately regulate pharmacies to prevent product contamination?

The Honorable Peter Welch

1. Currently, we understand there is a mechanism for compounding pharmacies to register with the FDA. What authority does this give the FDA over the pharmacies that voluntarily register with the FDA? What standards are enforced on these registered pharmacies?

The Honorable Gene Green

1. During the first round of questions you said that there are certain drugs that neighborhood compounders should not be making. Is that something FDA wants to be able to forbid with new authority?
2. Does the FDA currently not have the authority to regulate what drugs can be compounded?
3. Additionally, to clarify from earlier, you seemed to be saying that the FDA did not currently have the capacity to address all of the oversight it would like to over compounders, is that correct?
4. The FDA has said in the past that they did not have regulatory authority to further investigate NECC in advance of the outbreak. However, the FDA has inspected 31 facilities since the outbreak. In your testimony, you outline several other incidents, including one in Texas, which were the result of unsanitary compounds, what else has changed that the FDA believes it has inspection authority now, but did not previously?
5. Have all of the compounders that you have inspected willingly opened their doors to the FDA or, even in light of the recent tragedy, have there been some compounders that have challenged FDA's authority?
6. I'd like to hear more on the specifics of how the FDA will be able to use its new authority. Will it require user fees or some other type of fee paid by compounders in order to facilitate this authority?
7. Can we draw a bright line at whether the entity ships over state boundaries as the determining factor for the FDA to enter?
8. If we use other criteria in addition to interstate commerce, will that leave large loopholes or inadvertently exempt some compounders who should not be?