A CONTINUING INVESTIGATION INTO THE FUNGAL MENINGITIS OUTBREAK AND WHETHER IT COULD HAVE BEEN PREVENTED

HEARING

BEFORE THE

SUBCOMMITTEE ON OVERSIGHT AND INVESTIGATIONS

OF THE

COMMITTEE ON ENERGY AND COMMERCE

HOUSE OF REPRESENTATIVES

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[1] The document binder is available at http://docs.house.gov/meetings/if/if02/20130416/100668/hhrg-113-if02-20130416.xml.

A CONTINUING INVESTIGATION INTO THE FUNGAL MENINGITIS OUTBREAK AND WHETHER IT COULD HAVE BEEN PREVENTED

TUESDAY, APRIL 16, 2013

HOUSE OF REPRESENTATIVES,
SUBCOMMITTEE ON OVERSIGHT AND INVESTIGATIONS,
COMMITTEE ON ENERGY AND COMMERCE,
Washington, DC.

The subcommittee met, pursuant to call, at 10:02 a.m., in room 2123 of the Rayburn House Office Building, Hon. Tim Murphy (chairman of the subcommittee) presiding.

Members present: Representatives Murphy, Burgess, Scalise, Harper, Olson, Gardner, Griffith, Johnson, Long, Ellmers, Barton, Upton (ex officio) DeGette, Braley, Schakowsky, Butterfield, Tonko, Green, Dingell, and Waxman (ex officio).

Staff present: Gary Andres, Staff Director; Mike Bloomquist, General Counsel; Sean Bonyun, Communications Director; Matt Bravo, Professional Staff Member; Karen Christian, Chief Counsel, Oversight; Andy Duberstein, Deputy Press Secretary; Brad Grantz, Policy Coordinator, Oversight and Investigations; Debbee Hancock, Press Secretary; Sydne Harwick, Legislative Clerk; Brittany Havens, Legislative Clerk; Sean Hayes, Counsel, Oversight and Investigations; Carly McWilliams, Professional Staff Member, Health; Andrew Powaleny, Deputy Press Secretary; Krista Rosenthall, Counsel to Chairman Emeritus; Charlotte Savercool, Executive Assistant, Legislative Clerk; Alan Slobodin, Deputy Chief Counsel, Oversight; John Stone, Counsel, Oversight; Dan Tyrrell, Counsel, Oversight; Lyn Walker, Coordinator, Admin/Human Resources; Tom Wilbur, Digital Media Advisor; Phil Barnett, Democratic Staff Director; Stacia Cardille, Democratic Deputy Chief Counsel; Brian Cohen, Democratic Staff Director, Oversight and Investigations, Senior Policy Advisor; Eric Flamm, FDA Detailee; Elizabeth Letter, Democratic Assistant Press Secretary; Stephen Salsbury, Democratic Special Assistant; and Rachel Sher, Democratic Senior Counsel.

OPENING STATEMENT OF HON. TIM MURPHY, A REPRESENTATIVE IN CONGRESS FROM THE COMMONWEALTH OF PENNSYLVANIA

Mr. MURPHY. Good morning. This is a hearing of the House Energy and Commerce Oversight and Investigations Committee enti-

tled "A Continuing Investigation into the Fungal Meningitis Outbreak, and Whether it Could Have Been Prevented."

The subcommittee is here today because 53 people died from a pain medication manufactured by the New England Compounding Center, NECC. Those patients trusted that the steroid injected into their spine or their joints to relieve chronic pain was perfectly safe because of the confidence our Nation's healthcare providers place in the Food and Drug Administration. But that drug was contaminated with fungus, a form of mold that attacks bone and nerves.

More than 700 people who received these lethal injections continue to have symptoms. Today, they are living with the unbearable horror of not knowing whether they will survive. They must spend weeks in the hospital, missing work, holidays, and times with families. They must take large doses of morphine to ease the pain. Each day is lived under the deadly threat of an infection that could reach their brains and kill them.

This outbreak is one of the worst public health disasters in our country's history, and it is a terrible tragedy and an epic failure. Sadly, the Food and Drug Administration, which is supposed to protect the public, has spent its time passing blame and hiding behind judicial robes rather than taking any responsibility.

At our hearing last November, Commissioner Hamburg told this committee that the FDA faced "complex" issues in taking enforcement action against the New England Compounding Center.

Here is the truth: this outbreak begins with NECC illegally shipping 17,000 vials of supposedly sterile drugs without patient prescriptions. The FDA insists it could not tell the difference between a corner drug store compounder who makes cough syrup for a child, and a massive manufacturer illegally shipping into 23 states.

This committee has discovered the agency had information that should have spurred it to act and stop this rogue outfit from continuing to operate as an illegal manufacturer of sterile medication.

This outbreak is simply not "complex" nor was it a surprise. They were under the nose of the FDA for a decade. DA field staff and FDA headquarters repeatedly received complaints about NECC's numerous transgressions. They even considered additional inspections and enforcement. Ten years of warning signs, alarm bells, and flashing red lights were ignored. Complaints from patients, nurses, pharmacists, doctors, pain clinics, hospitals, drug companies, drug distributors and even confidential company informants, but the only healthcare entity that didn't seem worried was FDA headquarters. Ultimately, the FDA knew NECC was breaking the law but chose to do nothing.

In 2007, the FDA received complaints from patients getting epidural injections of an injectable steroid manufactured by NECC. FDA knew long ago that this very NECC product hospitalized patients with meningitis-like symptoms. These complaints led to FDA's first inspection of NECC, and this time, there is no evidence that FDA even bothered to inform the state or contact the company over this issue.

In 2011, a representative from the Institute of Safe Medication contacted the FDA. This complaint read, "As a practicing pharmacist, I am shocked that such a product would be allowed to be distributed for use in the United States." FDA officials found the

product to be "extremely dangerous," and "they should further warn that this bag should not be directly infused to the patient. This is unbelievable. I think this is a disaster waiting to happen."

After FDA headquarters approved, then rejected, sending a warning letter to Ameridose in 2009, the current Director of FDA's New England District Office angrily informed other enforcement officials with FDA: "I have told our Investigations Branch to not bother inspecting compounding pharmacies if we aren't going to act on the violations."

FDA's primary mission is to protect the public health from unsafe drug products. On numerous occasions, the agency confronted a choice in dealing with NECC and Ameridose: take action to protect patients or wait. Repeatedly, the FDA made a conscious decision to do nothing. In particular, under the watch of Dr. Hamburg, the FDA put enforcement actions against NECC and Ameridose on hold in 2011 and through 2012, because the FDA lawyers wanted to wait until finishing a revision of a guidance document.

During this inspection holiday, 53 people died.

At the last hearing Congressmen Terry, Scalise, and I asked Dr. Hamburg where in the law it said FDA could not act. The FDA did not answer our question. We now know that there was nothing in the law that prevented the FDA from acting because in the last few weeks before this hearing, the FDA has conducted a highly visible campaign of inspections. This flurry of well-publicized activity exposes the FDA's charade. The agency cannot argue it lacked authority to inspect NECC and Ameridose, but now, after the outbreak, has the authority to conduct these inspections. No law has changed. The only change is the FDA decided to act.

During our November hearing, Dr. Lauren Smith of the Massachusetts Department of Public Health recognized that her agency could have done things differently. She didn't hide behind ongoing investigations, lawsuits, or limited authority. Instead, she admitted that her agency had moved too slowly, and that if they had acted quickly in 2012, it could have prevented about a third of the deadly drug from being shipped. She took immediate personnel actions as a result of these conclusions.

The hope of this committee is that we will hear admissions from the FDA that reflect decisive leadership, an admission of what went wrong internally to delay inspections, warnings, and actions. What I worry about is we will hear this morning a continued litany of excuses, bureaucratic talk, and blame on outside organizations.

For the sake of the families of those who died, and those who are still sick, we will not stop in our effort to get answers and fix this problem.

[The prepared statement of Mr. Murphy follows:]

PREPARED STATEMENT OF HON. TIM MURPHY

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This Committee has discovered the agency had information that should have spurred it to act and stop this rogue outfit from continuing to operate as an illegal manufacturer of sterile medication.

This outbreak is not "complex" nor was it a surprise. Neither NECC nor its sister company, Ameridose, were operating in the shadows. They were under the nose of the FDA for a decade. FDA field staff and FDA headquarters repeatedly received complaints about NECC's numerous transgressions. They even considered additional inspections and enforcement actions. Ten years of warning signs, alarm bells, and flashing red lights were deliberately ignored. Complaints came from patients, nurses, pharmacists, doctors, pain clinics, hospitals, drug companies, drug distributors and even confidential company informants. About the only healthcare entity that didn't seem worried was FDA headquarters. Ultimately, the FDA knew NECC was breaking the law but chose to do nothing.

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The complaint read, quote, "As a practicing pharmacist, I am shocked that such a product would be allowed to be distributed for use in the United States." FDA officials found the product to be "extremely dangerous." A member of FDA's compounding team wrote: "And they should further warn that this bag should not be directly infused to the patient. This is unbelievable! I think this is a disaster waiting to happen."

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For the families of those who died, and those who are still sick, we will not stop in our effort to get answers and fix this problem.

I now recognize my distinguished colleague from Colorado, Ranking Member DeGette, for her opening statement.

Mr. MURPHY. I now recognize my distinguished colleague from Colorado, Ranking Member Diana DeGette, who I think also wants us to recognize some of the consent here, too.

Ms. DEGETTE. Thank you very much, Mr. Chairman. I know I join you and the rest of the members of this subcommittee in expressing our deepest condolences to those who are affected by the tragic events yesterday in Boston, and we are all thinking about all the victims. Our colleague, Mr. Markey, has been very interested in this investigation, and understandably, he is not here today, but he wanted to participate and he has a statement, and he also has an October, 2012 report that you folks have seen called "Compounding Pharmacies, Compounding Risk", and I ask unanimous consent those both be entered into the record.

Mr. MURPHY. Without objection, they will be entered into the record.

[The information appears in the document binder.]

OPENING STATEMENT OF HON. DIANA DEGETTE, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF COLORADO

Ms. DEGETTE. Thank you very much.

Mr. Chairman, I want to thank you for having today's hearing. Obviously, this fungal meningitis outbreak is a serious, serious situation, and our committee needs to understand the facts about how and why it occurred, and what we can do to prevent it in the future.

I think that this investigation has the potential to become part of the great bipartisan oversight history of this committee. I know that good investigations don't always result in legislative change, but in this case, I think we can use this investigation to help us identify the legislative changes, if any, that we need to help us avoid tragedies like this again in the future.

As hospitals, clinics, and other medical providers outsource more of their compounding, a number of compounding pharmacies have sprung up, and frankly, they have been operating underneath the regulatory radar screen. A spotty pattern of state regulations and enforcement, combined with conflicting federal law, have made that even worse.

So Mr. Chairman, I want to talk about some of the facts we have uncovered as we have spent the last 5 months investigating the New England Compounding Center, the FDA, and the deadly fungal meningitis outbreak caused by contaminated compounded drugs.

First of all, as we all can stipulate, the owners and operators of NECC ran a shoddy, fly-by-night operation, and jeopardized the

lives of thousands of people. Second, for several years prior to the outbreak, the FDA received warnings about the company from its own inspectors, from State Boards of Pharmacy, and from whistleblowers. The FDA received warnings about, and seriously considered investigating, Ameridose, NECC's sister company, just a few months before NECC began to ship the deadly steroid products. One of the states that discovered these deficiencies was my own home State of Colorado, and in fact, my State Board of Pharmacy issued a Cease and Desist Order to stop the company's practices.

Now, I am confident that we can all agree on these two facts from both sides of the aisle, but I also hope that we can agree on a third fact that will help explain why the FDA Was unable to effectively regulate this company. Then I hope that we can act together to fix the problem.

Mr. Chairman, in October of 2012, this committee requested thousands of pages of documents from the FDA about their interactions with NECC, and their approach to regulating compounded drugs. The Democratic staff has reviewed these documents, and yesterday released a supplemental memo with key findings. I would also ask unanimous consent that this memo be made a part of this hearing record.

This pattern of documents from 2002 through last year demonstrates that under two Administrations and over 10 years, the FDA has not been aggressive enough in attempting to regulate compounding pharmacies. The question is why? It is a serious and legitimate question to ask what the agency should have been doing and could have been doing over these many years, and I know from your opening statement you intend to do just that.

I also, though, look forward to hearing what specific solutions Commission Hamburg and the FDA believe would help them protect the American people from another outbreak, because these documents show us that for a year, the FDA has been grappling with a law that is broken and we need to help fix that law and keep the American public safe. We also need to look at how court decisions impacted the FDA's ability to regulate.

Mr. Chairman, you say that the FDA is hiding behind judicial robes, but in fact, court decisions are the law of the land. And what we have here in the wake of the serious meningitis outbreak is a patchwork of laws. We have two judicial circuits that are coming up with different decisions about the authority of the FDA, which is causing some of these compounding pharmacies, not all of them, but some of them to resist any regulatory efforts by the FDA.

As the FDA has been attempting to better regulate this situation since these issues came out, there have even been instances of compounding pharmacies refusing to provide the FDA access to records or facilities, and as we learned during our food safety investigations and some of our other investigations in this committee, if you have an allegation of little black particles in some of the vials of the pharmaceuticals, the FDA and its cooperating agencies need the ability to work fast. And if you have a company that says you can't come in here and makes the FDA go to court, that is not a speedy or a desirable resolution.

And so I am looking forward to hearing from Commissioner Hamburg about, number one, what the agency has done to improve

the situation and to improve enforcement, and number two, what the agency thinks that we need to do legislatively to fix this law so that this will never happen again.

Thank you very much, Mr. Chairman. I yield back.

Mr. MURPHY. Gentlelady yields back. I will now recognize the chairman of the full committee, Mr. Upton, for 5 minutes.

OPENING STATEMENT OF HON. FRED UPTON, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF MICHIGAN

Mr. UPTON. Well thank you, Mr. Chairman. I thank you for convening this very important hearing on the deadly outbreak of fungal meningitis so that the committee can get answers to the question that we could not get last year: what did the FDA know about NECC and Ameridose, and what did the FDA do about it?

When Commissioner Hamburg appeared before us last November, 32 innocent Americans had died. Today, the death toll stands at 53 and continues to grow. Hundreds are still sick and suffering. An unthinkable, public health disaster continues to get only worse. My home State of Michigan has been hit the hardest by fungal meningitis. According to the CDC, 15 of the 53 people who died after receiving NECC's contaminated products are from Michigan, including three from my district. Two hundred and fifty-nine of the 730 people who are sick and suffering from infections are from my state.

Just a few weeks ago, our Attorney General Bill Schuette, a former colleague, announced that he planned to convene a grand jury to investigate possible criminal charges, and I talked with him again just minutes ago.

Criminal cases will rightfully examine the company's liability for this tragedy, but it is our job at this committee to also take a hard look at the agency under our jurisdiction, the FDA, and ask: did its processes work? Did the agency do its job and protect the public's health? And before we get to the matter of additional authorities and new legislation, we have to ensure that the agency is going to be ready to implement them properly. It is not enough or right just to do something for the sake of doing it. We have to do something that is truly effective to prevent this from happening again.

It took months for the FDA to fully cooperate and provide the necessary documents, but now we finally have them. Commissioner Hamburg, as we look at these, many of us are troubled by what we have learned. FDA received complaint after complaint about these companies. FDA's documents paint a picture of two companies who appeared to be acting more like manufacturers than compounders. Doctors and other providers made complaints about the sterility of their products. FDA district staff pushed to go back out and re-inspect these companies or take other enforcement action, but in most cases, it simply didn't happen. It is this breakdown that concerns me the most. Job one for the FDA is making sure the medicines we take are safe, but the mission appears to be lost, as delays prevented the FDA from taking decisive action and the agency took years to finalize its guidance and regulatory documents. We know now that 53 Americans did not need to die. It sickens me that this could have been prevented.

And as we met this last week, I share your hope that this is a constructive hearing. We all want that. We need to get all the facts on the table, and I hope you can help us, so we can move forward. We owe it to those families, and I know that we can do better and work together.

And I yield now to Mr. Barton.

[The prepared statement of Mr. Upton follows:]

PREPARED STATEMENT OF HON. FRED UPTON

I thank Chairman Murphy for convening this important hearing on the deadly outbreak of fungal meningitis, so that this committee can get answers to the question we could not at the last hearing: what did FDA know about NECC and Ameridose? And what did FDA do about it?

When Commissioner Hamburg appeared before us last November, 32 innocent Americans had perished. Today, the death toll stands at 53 and continues to grow. Hundreds are still sick and suffering. An unthinkable, public health disaster keeps on getting worse. My home state of Michigan has been hit the hardest by the fungal meningitis outbreak. According to the CDC, 15 of the 53 people who died after receiving NECC's contaminated products are from Michigan, including 3 from my district. Two-hundred fifty-nine of the 730 people who are sick and suffering from infections are from my state. Just a few weeks ago, Michigan Attorney General Bill Schuette announced that he planned to convene a grand jury to investigate possible criminal charges.

Criminal cases will rightfully examine the company's liability for this tragedy. But it is our job at this committee to also take a hard look at the agency under our jurisdiction, the FDA, and ask: did its processes work? Did the agency do its job and protect the public health? Before we get to the matter of additional authorities and new legislation, we have to ensure that the agency is going to be ready to implement them properly. It is not enough or right just to do something for the sake of doing something. We have to do something that is truly effective.

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Commissioner Hamburg, we met last week. I share your hope that this is a constructive hearing. We need to get all the facts on the table, and I hope you will help us, so we can move forward. We owe it to the families who lost loved ones and we owe it to those 730 Americans who are still suffering and may never return to leading healthy lives. I yield my remaining time to....

Mr. BARTON. Thank you, Mr. Chairman, and I want to echo what you just said.

We have asked several questions at the previous hearing on this. The first one was how did this happen, and the second one, could this outbreak have been prevented? At the time, we didn't get answers. Finally after the committee has received the documents, we do have at least partial answers to those two questions.

To the first question, how did it happen, there are two main reasons. Obviously, the company involved acted negligently and didn't follow proper sterilization and sanitation practices, but number two, the FDA, the agency responsible for protecting the public health and safety, did not act properly, did not do what it should have done, and did not act when it could have acted. In fact, it

failed to take the necessary action against this company to prevent future outbreaks, even though they had evidence of serious problems dating back to 2002.

The answer to the second question, could the outbreak have been prevented, I believe the answer to be yes. I believe it could have been prevented. Today, we are going to have our FDA commissioner before us to explain the FDA's failure, and hopefully the steps that she is intending and hopefully has taken to prevent any future actions.

And with that, I yield the balance of the time to Dr. Burgess.

Mr. BURGESS. I thank the gentleman for yielding.

From a provider's perspective, I recognize the value of compounding pharmacies and compounding pharmacists, and that they contribute to the armamentarium of things that we can offer to our patients, but there is a vast difference between compounding preparation of progesterone to treat a condition, or compounding a pediatric elixir for Tamiflu, and being involved with a wholesale manufacturer of medicines that are shipped all over the country, with no specific prescription thereto attached. I do have to admit, reading through this litany that has occurred, honestly, before you arrived at the agency, but also since your arrival at the agency, and it is troubling. I think the least we can do today is try to uncover those things that were impediments to getting a rapid resolution of this, and honestly, we cannot allow it to happen again.

And I will yield back.

Mr. MURPHY. Gentleman yields back. I now recognize the ranking member of the committee, Mr. Waxman for 5 minutes.

OPENING STATEMENT OF HON. HENRY A. WAXMAN, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF CALIFORNIA

Mr. WAXMAN. Thank you, Mr. Chairman.

I think that the comments of Chairman Upton and Mr. Barton and Mr. Burgess are right on point. This has to be a constructive investigation. We have to know what happened and how to prevent it in the future.

This meningitis outbreak from compounded drugs has claimed the lives of over 50 people, sickened over 700, brought unspeakable grief upon hundreds of families, and it is one of our Nation's worst public health disasters in recent memory. So we need to get to the bottom of this.

Our most critical task is to answer this question: how can we prevent another NECC tragedy from occurring again? This one has happened. It is terrible.

Last fall, Joyce Lovelace, who lost her husband, courageously testified before this committee and we should heed her words. She said "Don't just investigate, instead, legislate and regulate. Put aside partisan politics, partisan philosophies, industry lobbying, and wishes of campaign contributions, and unanimously send to the White House a bill that will prevent a recurrence of these events. If you will do that, perhaps my family can take some solace in the fact that any Lovelace's public service continues even after death."

Well, I hope we can remember this advice during today's hearing, and stay focused on our most important mission: how can we prevent a recurrence of these events? The committee received in preparation for this hearing over 27,000 documents from the FDA. Mr. Chairman, I agree with your comments that the record shows that FDA missed important opportunities to address problems at NECC. FDA was warned about potential problems at NECC and Ameridose, and was simply unable to act or act fast enough. But the documents also show more than that. They show why this happened, and if we want to fix this problem, that is exactly what we need to understand.

Mr. Chairman, here is what the documents show. For over a decade, FDA struggled to effectively regulate compounding pharmacies. Basic flaws in the compounding law and a series of conflicting court decisions have created uncertainty and confusion. As a result, FDA was unable to develop a coherent policy. Under this Administration, beginning in 2009, FDA began to take new steps to develop an enforceable national policy for drug compounders, but it was never finalized. But this was difficult, because the court cases created different rules for different parts of the country, which is inherently problematic. FDA had to struggle with how to pick up the pieces of a statute in tatters.

Mr. Chairman, we should ensure that FDA is able to protect all of us in a uniform way from unsafe compounded drugs. It is Congress' job to fix the law when it is inadequate or when courts invalidate it, and that is why we must do more than blame the FDA for this tragedy. We must heed the words of Joyce Lovelace, and act to give the FDA the clear authority they need to keep the American public safe and prevent another drug compounding disaster.

I am pleased that Dr. Hamburg is here to further answer our questions. At the last hearing, a lot of the documents that our committee had requested on a bipartisan basis had not been received, and we now have those documents. And what we have is a muddied record of inaction where we would have liked to see action, clarity in the law to give you instructions, Dr. Hamburg, but that law wasn't clear and the courts made it even more confusing.

Our job is not to dwell on the confusion. Our job is to clarify what we want FDA to do, what we expect from FDA. We need to clarify it not just by criticism in an oversight hearing, but by acting together legislatively to spell out what the law must be in order for FDA to do everything it can to prevent another tragedy like this from occurring again.

Thank you, Mr. Chairman.

Ms. DEGETTE. Mr. Chairman, I would like to renew my unanimous request to put the Democratic memo in the record.

Mr. MURPHY. Without objection, so be it. Thank you.

[The information appears at the conclusion of the hearing.]

Mr. MURPHY. I would now like to introduce the Honorable Margaret A. Hamburg. She has been the commissioner of the U.S. Food and Drug Administration since May 18, 2009. She is an experienced medical doctor, scientist, and public health executive. Thank you for being here.

I also ask—let me go here. You are aware that the committee is holding an investigative hearing, and when doing so, has the practice of taking testimony under oath. Do you have any objections to testifying under oath?

Dr. HAMBURG. No, I do not.

Mr. MURPHY. The chair then advises you that under the rules of the House and rules of the committee, you are also entitled to be advised by counsel. Do you desire to be advised by counsel during your testimony today?

Dr. HAMBURG. I have with me Mr. Taylor, who is my senior counselor, and I would like him to be available to answer questions to give you the specific information that you might need.

Mr. MURPHY. Certainly. You have the right to have counsel there, too.

In that case, would you both please rise and raise your—one moment. Yes?

Ms. DEGETTE. Mr. Chairman, I don't believe that Dr. Hamburg is saying he is her lawyer, I think he is——

Dr. HAMBURG. Oh, I am sorry.

Ms. DEGETTE [continuing]. A lawyer at FDA here to answer questions. My suggestion would be to swear them both in.

Mr. MURPHY. We will swear them both in then, yes.

All right, if you both rise and raise your right hand, I will swear you in.

[Witnesses sworn.]

Mr. MURPHY. Let the record show that both have answered affirmatively, so you are now under oath and subject to the penalties set forth in Title 18, Section 1001 of the United States Code.

You may now give a 5-minute summary of your written statement, Dr. Hamburg.

TESTIMONY OF THE HONORABLE MARGARET A. HAMBURG, M.D., COMMISSIONER, U.S. FOOD AND DRUG ADMINISTRATION (FDA)

Dr. HAMBURG. Thank you very much, Mr. Chairman and members of the subcommittee. I am Dr. Margaret Hamburg, the Commissioner of the FDA. I appreciate the opportunity to testify today. I am joined, as I said, by Mr. John Taylor, my senior counselor, and former head of both our Drug Enforcement Office and of the agency's Field Inspection Force.

We are at a critical juncture for public health. The deadly outbreak of fungal meningitis associated with a compounded medication last fall was a horrible tragedy. I speak for everyone at the FDA when I say that our hearts go out to the victims and their loved ones.

While our investigation of this deadly outbreak has been a top priority, my responsibility is also to make sure that this does not happen again.

In looking at the history and our role with compounding pharmacies, it is clear to me that we should have more aggressively applied existing authorities, in spite of an ambiguous statute, a changing legal landscape, and continuous challenges by industry to our authorities. We are being more aggressive now. We are working with states to inspect pharmacies that we believe may present

the highest risk, in addition to responding to specific complaints we may receive. Over the past few months, we have conducted over 55 such inspections.

What we have seen is troubling: serious issues, including quality concerns that have led to product recalls, and practices that create risk of contamination, and these inspections have underscored our need for stronger, clearer authority to adequately protect public health. Even in light of the recent tragic events, astonishingly, some of the firms are challenging us, delaying our inspectors or denying them full access to records. In two recent instances, we have had to secure administrative warrants from the court and have U.S. marshals accompany our inspectors so they could complete their work. In other cases, we had to threaten the use of warrants to achieve cooperation.

Lack of clarity in our statutory authorities is not the only concern. The healthcare system and this industry have evolved tremendously. A new breed of pharmacy compounding—"outsourcers," has outgrown the legal framework. These outsourcers produce high volumes of high risk drugs, often for hospitals that rely on them to meet critical product needs for their patients.

The tools we have under current law for regulating these firms are simply not the right fit. Applying them in full force could lead to significant dislocations in the healthcare system, and likely shortages. We need legislation to preserve the benefits of traditional compounding, while at the same time giving us the right tools to regulate the highest risk practices and products. For these higher risk compounding pharmacies, we need legislation that: requires compliance with federal quality standards; requires federal registration so we know who they are, where they are, and what drugs they are making; and requires reporting to FDA of serious adverse events—so that we can act before potential problems grow out of hand.

For all pharmacy compounding, certain basic protections should be in place, including: clear authority to inspect records to determine the scope and nature of a pharmacy's operations, and to more quickly determine the cause of an outbreak; a prohibition on compounding of the most complex and highest risk products; and clear labeling of compounded drugs to allow prescribers and consumers to make more informed choices.

We look forward to working with Congress to explore funding mechanisms to support this oversight.

If you look at FDA's attempts to regulate pharmacy compounding over the last 20 years, as detailed in the tens of thousands of pages of documents we have provided to the committee, you see that the agency has been struggling with how to effectively oversee this industry. You see numerous approaches that were derailed by a constantly changing legal landscape, challenges to our authority, and conflicting court decisions. I wish that during my tenure I had brought the need for legislation to you sooner. To be frank, given the history of this issue and the efforts of this industry, there were many at the agency concerned that seeking new authority would result in a weakening, rather than a strengthening of the law. But I am here now to ask for your help. We have had an urgent call

to action. We are all on notice, and we owe it to the public and the victims to provide better protection in the future.

I am happy to answer any questions you may have.

[The prepared statement of Dr. Hamburg follows:]

DEPARTMENT OF HEALTH AND HUMAN SERVICES Public Health Service

Food and Drug Administration
Silver Spring, MD 20993

STATEMENT

OF

MARGARET A. HAMBURG, M.D.

COMMISSIONER OF FOOD AND DRUGS

FOOD AND DRUG ADMINISTRATION

DEPARTMENT OF HEALTH AND HUMAN SERVICES

BEFORE THE

SUBCOMMITTEE ON OVERSIGHT AND INVESTIGATIONS
COMMITTEE ON ENERGY AND COMMERCE

U.S. HOUSE OF REPRESENTATIVES

"A CONTINUING INVESTIGATION INTO THE FUNGAL MENINGITIS OUTBREAK AND WHETHER IT COULD HAVE BEEN PREVENTED"

April 16, 2013

RELEASE ONLY UPON DELIVERY

INTRODUCTION

Mr. Chairman and Members of the Subcommittee, I am Dr. Margaret Hamburg, Commissioner of Food and Drugs at the Food and Drug Administration (FDA or the Agency), which is part of the Department of Health and Human Services (HHS). Thank you for the opportunity to be here today to discuss important issues related to pharmacy compounding.

We are at a critical point where we must work together to improve the safety of drugs produced by compounding pharmacies. As the compounding industry has grown and changed, we have seen too many injuries and deaths over many years caused by unsafe practices. I testified in front of this Subcommittee on November 14, 2012, soon after the emergence of a tragic fungal meningitis outbreak associated with compounded methylprednisolone acetate (MPA), a steroid injectable product distributed by the New England Compounding Center (NECC). To date, that outbreak has resulted in 51 deaths and over 730 people sickened in 20 States. Sadly, NECC was not an isolated incident. Indeed, over the past 20 years we have seen multiple situations where compounded products have caused deaths and serious injuries. For example, in 2001, 13 patients in California were hospitalized and 22 received medical care following injections from contaminated vials of a steroid solution. Three patients died as a result. In 2005, contaminated cardioplegia solution resulted in five cases of severe system inflammatory infections; three of these patients died. In 2007, three people died from multiple organ failure after a Texas compounder sold superpotent colchicine that was as much as 640 percent the labeled strength. In 2011, there were 19 cases of *Serratia marcescens* bacterial infections, including nine deaths, associated with contaminated total parenteral nutrition products, and in 2012, 43 patients developed fungal eye infections from contaminated sterile ophthalmic drug products. At least 29 of these patients suffered vision loss. These incidents are emblematic of long-standing issues

associated with the practice of compounding and the public health concerns that can result from unsafe practices in compounding pharmacies.

Since the NECC outbreak, there have been seven additional recalls of sterile compounded and repackaged drug products by different pharmacies. In one very recent incident, the presence of floating particles, later identified to be a fungus, was reported in five bags of magnesium sulfate intravenous solution, resulting in a nationwide recall of all sterile drug products produced by the pharmacy (over 100 products). Fortunately, we have not received reports of patient injury from these products. In another recent recall, all sterile drug products (approximately 60 products) from a second pharmacy were recalled as a result of reports that five patients were diagnosed with serious eye infections associated with the use of repackaged Avastin. Moreover, we believe that presently, there are hundreds of other firms operating as compounding pharmacies, producing what should be sterile products and shipping across State lines in advance of or without a prescription. However, the current legal framework does not provide FDA with the tools needed to identify and adequately regulate these pharmacies to prevent product contamination.

The history of this issue shows that there is a need for appropriate and effective oversight of this evolving industry. It is clear that the industry and the health care system have evolved and outgrown the law, and FDA's ability to take action against compounding that exceeds the bounds of traditional pharmacy compounding and poses risks to patients has been hampered by gaps and ambiguities in the law, which have led to legal challenges to FDA's authority to inspect pharmacies and take appropriate enforcement actions.

The fungal meningitis outbreak has caused the Agency to review our past practices with regard to our oversight of compounding pharmacies, and has led to some preliminary conclusions. In my view, even in the face of litigation and continuous challenges by industry to our authorities, we can nonetheless be more aggressive in pursuing enforcement actions against compounding pharmacies within our current limited authority. I can assure you that we are being more aggressive now. We have established an Agency-wide steering committee to oversee and coordinate our efforts, and we have taken several important steps to identify and inspect high-risk pharmacies that are known to have engaged in production of sterile drug products.

Using a risk-based model, we identified 29 firms for priority inspections focused on their sterile processing practices. During these 29 inspections, in two instances, FDA identified secondary firms associated with the priority inspections, for a total of 31 firms. We have taken investigators who would normally be doing inspections of conventional drug manufacturers and assigned them to conduct inspections of those pharmacies whose history suggests a greater risk of potential quality issues with their compounded products. We have coordinated our inspections with State officials, who have accompanied our investigators in most cases. At the same time, we have also continued to conduct for-cause inspections, often at the request of our State counterparts who invited us to accompany them on the inspections. When we identified problems during any of the inspections, at the close of the inspection, we issued an FDA Form 483[1] listing our inspection observations. Thus far, we have issued an FDA-483 at the close of 43 of the 55 inspections we have conducted since last fall. We have seen some serious issues, including quality concerns that have led to product recalls. Observations have included: lack of

[1] A form FDA-483 is issued when investigators observe any significant objectionable conditions. It does not constitute a final Agency determination of whether any condition is in violation of the Federal Food, Drug, and Cosmetic Act (FD&C Act) or any of our relevant regulations, but the observations often serve as evidence of a violation of the FD&C Act and its implementing regulations.

appropriate air filtration systems, insufficient microbiological testing, and other practices that create risk of contamination.

Notably, even in light of recent events, and even though we are often working with the State inspectors, our investigators' efforts are being delayed because they are denied full access to records at some of the facilities they are inspecting. Just during the recent inspections, several pharmacies delayed or refused FDA access to records, and FDA had to seek administrative warrants in two cases. And although we have been able to eventually conduct the inspections and collect the records that we have sought, our ability to take effective regulatory action to obtain lasting corrective action with regard to substandard sterility practices remains to be seen.

As we have noted in the past, our ability to take action against inappropriate compounding practices has been hampered by ambiguities regarding FDA's enforcement authority, legal challenges, and adverse court decisions, and we have learned that the law is not well-suited to effectively regulate this evolving industry. For example, hospitals have come to rely on compounding pharmacies that function as "outsourcers" producing sterile drugs previously made by hospital in-house pharmacies. If FDA brings charges against a pharmacy, alleging that it is manufacturing a "new drug" that cannot be marketed without an approved application, the pharmacy will have to either obtain individual patient-specific prescriptions for all of its products or stop distributing the products until it obtains approved new drug applications for them, something most outsourcers are unlikely to do. Several of the pharmacies FDA inspected are some of the largest outsourcers in the country. These pharmacies supply large numbers of sterile drugs produced in relatively large quantities to hospitals nationwide, and a shut-down at these firms is likely to cause disruptions in the supply of drugs to hospitals and other health care

providers. FDA should have more tailored authorities appropriate for this type of compounding pharmacy.

In my last appearance before this Subcommittee, I presented a framework that could serve as a basis for the development of a risk-based program to better protect the public health, improve accountability, and provide more appropriate and stronger tools for overseeing this evolving industry. We have since met with over 50 stakeholder groups, including pharmacy, medical, hospital, payer, and consumer groups, and State regulators, to help further our understanding and inform our framework. Today, I will first provide background on FDA's current legal authority over compounded drugs, then provide additional details about the framework and suggest specific actions that Congress can take to help us better do our job and prevent future tragedies like this one.

FDA's Legal Authority over Compounded Drugs

FDA regards traditional pharmacy compounding as the combining or altering of ingredients by a licensed pharmacist, in response to a licensed practitioner's prescription for an individual patient, which produces a medication tailored to that patient's special medical needs. In its simplest form, traditional compounding may involve reformulating a drug, for example, by removing a dye or preservative in response to a patient allergy. It may also involve making an alternative dosage form such as a suspension or suppository for a child or elderly patient who has difficulty swallowing a tablet. FDA believes that pharmacists engaging in traditional compounding provide a valuable medical service that is an important component of our health care system. However, by the early 1990s, some pharmacies had begun producing drugs beyond what had historically been done within traditional compounding.

After receiving reports of adverse events associated with compounded medications, FDA became concerned about the lack of a policy statement on what constituted appropriate pharmacy compounding. In March 1992, the Agency issued a Compliance Policy Guide (CPG), section 7132.16 (later renumbered as 460.200) to delineate FDA's enforcement policy on pharmacy compounding. It described certain factors that the Agency would consider in its regulatory approach to pharmacies that were producing drugs.

The compounding industry objected to this approach and several bills were introduced, some with significant support, to limit the Agency's oversight of compounding.[2] In November 1997, S. 830, the Food and Drug Administration Modernization Act of 1997 (FDAMA), was signed into law as Public Law 105-115.[3] FDAMA added Section 503A to the FD&C Act, to address FDA's authority over compounded drugs.[4] Section 503A exempts compounded drugs from three critical provisions of the FD&C Act: the premarket approval requirement for "new drugs"; the requirement that a drug be made in compliance with current good manufacturing practice (cGMP) standards; and the requirement that the drug bear adequate directions for use, provided certain conditions are met. These provisions were the subject of subsequent court challenges, which have produced conflicting case law and amplified the perceived gaps and ambiguity associated with FDA's enforcement authority over compounding pharmacies. In 2002, immediately after a Supreme Court ruling that invalidated the advertising provisions of Section 503A, FDA issued a revised compliance policy guide on compounding human drugs. Several additional legal challenges and court decisions then followed. More recently, FDA made

[2] H.R. 5256, Pharmacy Compounding Preservation Act of 1994, introduced Oct. 7, 1994, 1 co-sponsor; H.R. 598, Pharmacy Compounding Preservation Act of 1994, introduced Jan. 20, 1995, 141 co-sponsors; H.R. 3199, Drug and Biological Products Reform Act of 1996, introduced March 29, 1996, 205 co-sponsors; H.R. 1060, Pharmacy Compounding Act, introduced March 13, 1997, 152 co-sponsors; H.R. 1411, Drug and Biological Products Modernization Act of 1997, introduced April 23, 1997, 16 co-sponsors

[3] Public Law 105-115, FDAMA, 111 Stat. 2296 (Nov. 21, 1997), available at *http://www.gpo.gov/fdsys/pkg/PLAW-105publ115/pdf/PLAW-105publ115.pdf*

[4] Id.

significant progress toward issuing another CPG. In fact, FDA was on track to publish a revised draft CPG in the fall of 2012, but the fungal meningitis outbreak intervened and we are now reevaluating the draft. It is important to note, however, that a CPG is not binding on industry and updating the CPG would not alleviate all issues with Section 503A.

A look at FDA's attempts to address compounding over the last 20 years shows numerous approaches that were derailed by constant challenges to the law. As a result, presently, it is unclear where in the country Section 503A is in effect, and Section 503A itself includes several provisions that have impeded FDA's ability to effectively regulate pharmacy compounding practices including those relating to prescription orders, medical need, and copying FDA-approved products.

Apart from Section 503A, there are additional provisions in the statute that have impeded effective pharmacy compounding regulation. For example, if certain criteria are met, the FD&C Act exempts compounding pharmacies from registration and the obligation to permit access to records during an inspection. As a result, FDA has limited knowledge of pharmacy compounders and compounding practices and limited ability to oversee their activities.

Looking Ahead

The Administration is committed to working with Congress to address the threat to public health from gaps in authorities for effective oversight of certain compounding practices. To that end, FDA has developed a framework that could serve as the basis for the development of a risk-based program to protect the public health.

Risk-based Framework

Recognizing the history of compounding practice, FDA supports the long-standing policy that all compounding should be performed in a licensed pharmacy by a licensed pharmacist (or a licensed physician), and that there must be a medical need for the compounded drug.

Further, we believe there should be a distinction between two categories of compounding: traditional and non-traditional. Traditional compounding would include the combining, mixing, or altering of ingredients to create a customized medication for an individual patient with an individualized medical need for the compounded product, in response to a valid patient-specific prescription or order from a licensed practitioner documenting such medical need. Traditional compounding, while posing some risk, plays an important role in the health care system, and should remain the subject of State regulation of the practice of pharmacy.

Non-traditional compounding would include certain types of compounding for which there is a medical need, but that pose higher risks. FDA proposes working with Congress to define non-traditional compounding based on factors that make the product higher risk such as any sterile compounding in advance of or without receiving a prescription, where the drug is distributed out of the state in which it was produced. Non-traditional compounding would be subject to Federal standards adequate to ensure that the compounding could be performed without putting patients at undue risk, and FDA would inspect against and enforce these Federal standards. Such a definition focuses on the highest risk activities and offers a uniform degree of protection across all 50 States, for highest-risk compounding activities.

Non-traditional compounding should, because of the higher risk presented, be subject to a greater degree of oversight. Sterile products produced in advance of or without a prescription and shipped interstate should be subject to the highest level of controls, established by FDA and

appropriate to the activity, similar to cGMP standards applicable to conventional drug manufacturers.

In addition, FDA believes that with noted exceptions, certain products are not appropriate for compounding under any circumstances. These products would include: 1) what are essentially copies of FDA-approved drugs, absent a shortage justification based on the drug appearing on FDA's shortage list; and 2) complex dosage forms such as extended release products; transdermal patches; liposomal products; most biologics; and other products as designated by FDA. Producing complex dosage forms would require an approved application and compliance with cGMP standards, along with other requirements applicable to manufactured drug products.

FDA believes that there are other authorities that would be important to support this new regulatory paradigm. For example, FDA should have clear ability to collect and test samples of compounded drugs and to examine and collect records in a compounding pharmacy, just as the Agency does when inspecting other manufacturers. FDA should also have clear ability to examine records such as records of prescriptions received, products shipped, volume of operations, and operational records such as batch records, product quality test results, and stability testing results. Such inspections are necessary to determine when a pharmacy exceeds the bounds of traditional compounding, to respond to public health threats, and to enforce Federal standards.

FDA also believes that an accurate inventory of pharmacies engaged in non-traditional compounding would facilitate appropriate oversight and coordination with State regulators. In addition, FDA looks forward to working with the Congress on potential improvements that may include label statements and adverse event reporting that have proven useful in other areas, A

user-fee-funded regulatory program may be appropriate to support the inspections and other oversight activities outlined in this framework. We look forward to working with Congress to explore the appropriate funding mechanisms to support this work, which could include registration or other fees, as Congress has authorized and FDA has successfully implemented in other settings.

CONCLUSION

Given our experiences over the past 20 years and the recent fungal meningitis outbreak, we must do everything we can to clarify and strengthen FDA's authority in this area. We recommend that Congress recognize the appropriate State role in regulation of traditional compounding while authorizing clear and appropriate Federal standards and oversight needed for non-traditional compounders that produce riskier products. We look forward to working with Congress in striking the right balance.

I am happy to answer any questions you may have.

Mr. MURPHY. I thank you for your testimony, Commissioner Hamburg, and I appreciate you want to move forward, but we also would like to find out if there are things within the FDA that has been going on for the last 10 years that need to be addressed first.

So I am assuming you accept that the buck stops with you with regard to how things are going with the FDA, am I correct?

Dr. HAMBURG. Yes.

Mr. MURPHY. OK. Now the FDA documents show that the FDA put enforcement actions against NECC and Ameridose on hold in 2011 through 2012, and suspended all inspections of compounders because the FDA wanted to issue new guidance first. For example, On October 24 of 2011, e-mail from a compliance officer in the FDA's district office to the district compliance branch director shows that in light of the FDA process of drafting guidance on compounding, the FDA inspectors did not immediately follow up on an informant's allegations about Ameridose. Salespeople were in the clean area, filling product, and that Ameridose continued to repack without an FDA license. The e-mail stated that Tamara Ely, the compounding team leader from CDER, said "no compounding facility is slated to be inspected in 2012," and a September, 2011, e-mail from a compliance officer at CDER to others in the FDA headquarters stated "the plan is to re-inspect Ameridose 6 months after issuance of 503A guidance." Likewise, an October, 2011, memorandum from the Office of Unapproved Drugs and Labeling Compliance stated "currently we have suspended inspections of compounding facilities, but will reinstate proactive inspections based on a risk model 3 to 6 months after the finalization of the guides to the industry."

Did you personally approve of the FDA decision to delay or suspend enforcement actions or inspections of compounding facilities, or did somebody else?

Dr. HAMBURG. I was not directly involved in those decisions, but they did reflect the concern that we needed to really have a clear regulatory regime that was outlined so that we could bring the strongest and best possible cases.

Mr. MURPHY. So were they then implemented under your knowledge? If you were not the decision-maker, were they implemented under your knowledge that they were occurring?

Dr. HAMBURG. I was not aware of those decisions.

Mr. MURPHY. Were you personally advised at any time about suspending enforcement actions against compounders back in 2011?

Dr. HAMBURG. It is important to understand that there were ongoing responses with the compounding industry when problems were brought to our attention about specific products, but that in terms of a proactive inspectional strategy, we did not have the framework in place and we were trying to put that in place with the development of the CPG.

Mr. MURPHY. I appreciate that, but we are trying to find out when were you informed about the policy to suspend any enforcement actions and inspections of compounders?

Dr. HAMBURG. I regret that I was not more fully aware, but I——

Mr. MURPHY. When did you find out? Do you recall when you finally found out that there were no inspections? Do you recall when that was?

Dr. HAMBURG. I want to make clear that there were inspections of compounding facilities in reaction to specific issues that were——

Mr. MURPHY. Well, with NECC and——

Dr. HAMBURG [continuing]. Brought before us with adulterated or other problems with products, but that there was not—there was this effort going on within the agency to try to develop——

Mr. MURPHY. I understand that. I am just trying to help focus here, because I read you quotes from e-mails of at least three different people that the inspections of NECC and Ameridose were suspended. It is an important decision. Had the FDA taken enforcement actions, conducted its own inspections, or caused the Massachusetts Board of Pharmacy to inspect, we may have been able to prevent this huge public health disaster. So when the FDA made the decision to suspend compounding enforcement in 2011, did the FDA weigh the potential public health consequences of that decision?

Dr. HAMBURG. It was not a decision to suspend all enforcement of compounding pharmacies——

Mr. MURPHY. I know, just with——

Dr. HAMBURG [continuing]. But I regret that we didn't do more, and I regret that I was not more directly engaged——

Mr. MURPHY. I appreciate that.

Dr. HAMBURG [continuing]. But I am now and——

Mr. MURPHY. I know.

Dr. HAMBURG [continuing]. And I really hope——

Mr. MURPHY. I am still trying to find out when did you find out that inspections of NECC were suspended?

Dr. HAMBURG. I do not recall specifically but I was not aware at that time.

Mr. MURPHY. Was it in preparation for the hearing in the fall or this hearing that you finally found out that the inspections hadn't been taking place?

Dr. HAMBURG. I as Commissioner obviously am not aware of all of the inspections we are doing. We are responsible for regulating products that come from over 300,000 different facilities——

Mr. MURPHY. I am just asking about NECC and I am not getting an answer, but that is important because something—it appears what has happened with NECC, that the information was not going to the top where the buck is supposed to stop, and while you are telling us that you didn't have authority to inspect, last week a flurry of publicity came out that you went to 31 different places. CBS News did an interview with you, and only one of those was someone questioned about a court order. So we still are going to need to get some answers to that, but I see my time is up so I am now going to recognize the Ranking Member, Ms. DeGette.

Ms. DEGETTE. Thank you very much, Mr. Chairman.

Commissioner Hamburg, did you ever find out why they inspected—why they suspended these inspections while they are writing new guidance? Why couldn't they walk and chew gum at the same time?

Dr. HAMBURG. There was, I think, real concern given the history with this issue, and the repeated challenges to our authorities that we needed to really understand, as court decisions were coming down, what were going to be the legal—what was the legal framework under which we would be——

Ms. DEGETTE. So they were afraid that they might not have the authority to do the inspections? Is that what you are saying?

Dr. HAMBURG. We have the authority to do the inspections——

Ms. DEGETTE. So why couldn't they do both at once?

Dr. HAMBURG [continuing]. But inspections are just a piece of what needs to be done to take enforcement actions, and

Ms. DEGETTE. Right, so you don't know why they didn't do both, because you didn't know at the time? Is that what you are saying? Why didn't they both do the inspections and write the new guidelines?

Dr. HAMBURG. I wish that there had been a more aggressive approach in terms of inspections.

Ms. DEGETTE. But you don't know why?

Dr. HAMBURG. There was an effort to follow up on specific concerns. That doesn't always require an inspection. But the desire was to—the CPG was being worked on in order to really provide clear guidance about the standards under which we would be looking at enforcement in these facilities, and I wish it had been completed more quickly and I——

Ms. DEGETTE. OK. So you testified now that this is at your level, the last number of months since November have been aggressively trying to go in and inspect, and that various companies have tried—have refused entry and you had to get court orders and so on. Very briefly, can you tell me how long it took you—it took the FDA from the time that you announced you wanted to go in and inspect to get these orders to get the marshals in? Was there a delay because of the resistance of the compounding pharmacies?

Dr. HAMBURG. Yes, there have been a variety of delays in terms of——

Ms. DEGETTE. But how long were those delays?

Dr. HAMBURG. Days to weeks.

Ms. DEGETTE. Days to weeks, OK. Now, are you saying—this is a really pretty simple question. Are you saying that the FDA should have the authority to regulate all drug compounders?

Dr. HAMBURG. We believe that we need to focus on those compounders that are making the highest risk products, the sterile products, in advance or without a prescription and shipping to other states. We believe that there are not sufficient standards in place in the law and enforceable——

Ms. DEGETTE. So it is really a targeted group of compounders that are engaged in interstate commerce that the FDA believes that need stronger authority, is that correct?

Dr. HAMBURG. We believe we need to focus on the highest risk facilities, and that includes those making sterile products and shipping——

Ms. DEGETTE. And what percentage of all the drug compounders is that?

Dr. HAMBURG. Well, we don't really know because we don't know——

Ms. DEGETTE. Because you don't have the authority——

Dr. HAMBURG [continuing]. Those compounders because they are not required to register with us, and we don't have full access to their records for assessment.

Ms. DEGETTE. Right. Now let's talk about this court case thing, because some people on this committee seem to think this is more important than others.

Now in 2001, the Ninth Circuit Court found that part of the 1997 Food and Drug Administration Modernization Act was unconstitutional, correct?

Dr. HAMBURG. Correct.

Ms. DEGETTE. And so—and then in 2002, the Supreme Court affirmed that decision about the constitutionality. Is that right?

Dr. HAMBURG. Correct.

Ms. DEGETTE. And then in 2008, there was a different circuit court that reached a different conclusion, finding that the key parts of the 1997 drug compounding law could remain in effect. Is that correct?

Dr. HAMBURG. That is correct.

Ms. DEGETTE. And is that that map that your staff put up over there? That looks to me like the map that shows, so in other words, in the red, that is one of the court decisions. In the blue, that is the other court decision, right?

Dr. HAMBURG. Correct.

Ms. DEGETTE. And then in the gray, that is the rest of the country that is covered by different courts that have not ruled on this, right?

Dr. HAMBURG. Correct.

Ms. DEGETTE. And so the result of this has been that the—is that the industry has pushed back against the FDA's attempts to regulate, right?

Dr. HAMBURG. Correct.

Ms. DEGETTE. Now, I think you do understand and I think you recognize we are not saying here that this absolves the FDA from responsibility to try, and you believe the FDA does have the responsibility to try to enforce to make sure that these compounding pharmacies are doing the right thing, right?

Dr. HAMBURG. Absolutely.

Ms. DEGETTE. But nonetheless, there is not a clarity in the law, and that is hampering the FDA to know clearly what it should do and to do it in a quick fashion. Is that right?

Dr. HAMBURG. That is absolutely correct.

Ms. DEGETTE. OK, thank you very much, Mr. Chairman.

Mr. MURPHY. I now recognize Mr. Barton for 5 minutes.

Mr. BARTON. Thank you, Mr. Chairman.

Madam Commissioner, I was puzzled as I listened to you evade the answer to the chairman's questions about when you learned. You never gave him a straight answer, so I am going to ask a question and let's see if we can get a straight answer.

Does the sun rise in the east, Madam Commissioner?

Dr. HAMBURG. You have me so confused, I don't know.

Mr. BARTON. Well, I would hope that we could have gotten a straight answer from that.

Dr. HAMBURG. No, yes.

Mr. BARTON. My seven-year-old would know the answer to that in the first grade, so if we have now established that you can give us some straight answers, I will give you once more chance to answer the chairman's question, when did you learn about all this? When did you become aware? Just a date, a time.

Dr. HAMBURG. You know, many of the issues that are involved here I did become aware of in the course of the investigation and reviewing the many documents that——

Mr. BARTON. Why are you afraid to just tell us?

Dr. HAMBURG. Because I am not—I really don't remember. Compounding pharmacies were an issue that——

Mr. BARTON. OK, well that is an answer.

Dr. HAMBURG [continuing]. I was not, deeply——

Mr. BARTON. If you don't remember, you really don't remember.

Dr. HAMBURG. And I regret it.

Mr. BARTON. So we will assume that you really, really don't remember.

So I am going to ask you another question. You have been the commissioner, I think for a little over 4 years, since you got confirmed by the Senate, so when you found out about this problem, how did you feel then and how do you feel now?

Dr. HAMBURG. When the meningitis outbreak began, like all of you, I was deeply concerned and committed the resources of our agency to engaging in the public health investigation and response, and I have been deeply involved in the subsequent activities, and I do believe we need to be more aggressive, and I intend to be more aggressive.

Mr. BARTON. I am asking for the—all the people of America that depend on the FDA, the gold standard of regulatory authority in the world. You are the point person. Obviously there are thousands of people at the FDA and you can't be personally responsible for each and every one of their actions, but in our form of government, you are the person that the President of the United States, confirmed by the Senate, is the leader. Are you upset with what this company did? Are you outraged? Are you confused? Are you puzzled? I mean, how do you feel?

Dr. HAMBURG. I am deeply troubled and I am committed to working with all of you, with industry, and with the states in order to ensure that we have the regulatory framework that we need in order to be able to best protect the health of the American people and ensure the safety of their health.

Mr. BARTON. All right.

Dr. HAMBURG. We do not presently have that in place, and I am worried that if we don't work together to address it, there may be future problems of this magnitude.

Mr. BARTON. OK, deeply troubled and worried. OK, that is—I find that acceptable.

Now, at our first hearing there was a lot of ping-pong balling back and forth whether it was a state problem, a state regulatory problem, or a federal regulatory problem, and I believe you testified that you needed more authority, and there was some ambiguity in the law, things like this. Since that time, you have shut the company down. I think there is a criminal case against the company. So obviously, the FDA had enough authority to do what it has

done. Do you, today, think that the authority is adequate on the books for your agency, or do you continue to believe that you need more authority?

Dr. HAMBURG. My understanding is that it was the state authority that was able to—NECC was licensed by the State of Massachusetts and it was the state authority that enabled——

Mr. BARTON. But my question is knowing what you know now, do you still want this committee to give the FDA additional authority, or are you satisfied that your agency, the FDA, has sufficient authority to do its job?

Dr. HAMBURG. We definitely need additional authorities. At the present time, compounding pharmacies under existing law, despite the ambiguities and the split court decision, compounding pharmacies are not required to register with us, so we don't know who they are and what they are making. They are not required—these large compounding pharmacies that are making sterile products are not required in law to——

Mr. BARTON. OK, so you think you need additional——

Dr. HAMBURG [continuing]. Apply uniform standards——

Mr. BARTON. My time is expired and I have one more question that I want to ask. Do you feel that this company is typical of the average compounding pharmacy?

Dr. HAMBURG. You know, I cannot—there is an ongoing criminal investigation, as you know. I can't comment on the specifics, but there are good players and bad players out there, compounding drugs. Compounding plays a critical role in our healthcare system, but we need to make sure that there are the standards in place and that FDA has the authorities to enforce those standards that will assure the quality and safety of these products, particularly these highest risk sterile products.

Mr. BARTON. I thank the commissioner and thank the chairman.

Mr. MURPHY. Thank you. Mr. Waxman is now recognized for 5 minutes.

Mr. WAXMAN. Thank you, Mr. Chairman.

Dr. Hamburg, if a manufacturer wants to produce a drug, they have to go to FDA and get approval and show the drug is safe and effective, and you keep track of those manufacturers, or even inspect some of their facilities, isn't that right?

Dr. HAMBURG. That is correct.

Mr. WAXMAN. So a compounding pharmacy can put together drugs, but they don't have to come to the FDA to ask approval or even register with you to let you know that they are doing that, isn't that correct?

Dr. HAMBURG. That is the case.

Mr. WAXMAN. They go to their states and have to let the states know, or does that depend on state law?

Dr. HAMBURG. State laws are very variable, as well as the resources for enforcement.

Mr. WAXMAN. Well, some people have said that because recently you have gone out and done inspections, between February and April of this year, of 30 compounding pharmacies that make sterile injectable drugs, and that there are inspections on occasion, that you have all the authority you need. Dr. Hamburg and Mr. Taylor, can you say that you have the authority to be able to comprehen-

sively oversee and inspect this industry that can act without your approval and maybe even in occasions you don't even know who they are?

Dr. HAMBURG. No, we, as you note, don't have the authority to even know who is out there and what they are making. We don't have those uniform national standards for safe practices, good manufacturing practices to inspect against and hold them to. They do not have to report adverse events that they might hear about to us so we can respond rapidly. This is not a system that is adequate to protect in the light of this changing healthcare system and its needs, and this evolving industry.

Mr. WAXMAN. The inspections that you have done are based on what information?

Dr. HAMBURG. We determined who to inspect based on either past awareness of concerns, public information about concerns, concerns states had brought to our attention, but we were inspecting companies that made sterile products because we view them as the highest risk, and we have certainly found considerable concerns about ongoing sterility practices, and we have also found that even in light of recent events, that companies are questioning our authorities to do full inspections, and the appropriateness of the inspections.

Mr. WAXMAN. When FDA wanted to look at this NECC, the company that made the drug that has done so much harm, in December of 2006—before you were there—FDA sent them a warning letter highlighting a series of violations of federal law, and this company responded in part that it didn't need FDA approval before dispensing compounded medications, and further, did not operate in a manner that would subject us to FDA regulation. In other words, they were resisting FDA doing its job. They were emboldened. Didn't that make your job even tougher?

Dr. HAMBURG. Well, it certainly has made it tougher. It has made it much less effective and efficient, and I think it speaks to the reason why I am here now, really asking for the chance to work with you to put in place the systems of legal and regulatory requirements that will enable better cooperation——

Mr. WAXMAN. I appreciate that.

Dr. HAMBURG [continuing]. And coordinating.

Mr. WAXMAN. Now if you find that pharmacy compounder and they are doing high risk work and you have some suspicions that there are problems and you want to do an inspection, can you get their records?

Dr. HAMBURG. We cannot always get their records.

Mr. WAXMAN. Well, you don't have the authority to get record inspections, isn't that right? The reason I say that is that at the Senate hearing in November, the compounding industry witness said FDA doesn't need new records inspection authority because it can access pharmacy records by getting a warrant.

Mr. Taylor, what does it mean, you have to go get a warrant if you want to see their records?

Mr. TAYLOR. Yes, so it is—once a refusal has occurred, what you actually have to do is put together essentially an affidavit that you would take to court explaining why you are seeking this warrant. Then an FDA employee would testify to the truth of the warrant,

and you actually have to bring it to a federal court judge. So it is——

Mr. WAXMAN. Well let me just stop you and say if we want you to do your job, we have got to give you the tools. We would rather make the law clear, and one ought to be you can do inspections and you can get these records and not have to go through the whole rigmarole where they want to fight you and have to go and get a warrant. Some cooperate, but some, especially those we are most suspicious of, can force you to go to court and get a warrant. Isn't that right?

Mr. TAYLOR. That is correct.

Mr. WAXMAN. Well, I hope we take that into consideration, Mr. Chairman, in addressing this question of the law that needs to be adopted by the Congress.

Mr. MURPHY. Thank you. Gentleman yields back, and I now recognize Dr. Burgess for 5 minutes.

Mr. BURGESS. I thank the chairman for the recognition. Dr. Hamburg, as always, welcome back to our humble committee room here in the Energy and Commerce Committee.

You know, I just have to say, reading through the information that was provided by your office that the staff has assembled, I mean, your staff must be some of the most frustrated people in the world, because it seems like they were always coming right up to the point where someone could pull the plug on NECC, on the New England Compounding Center, and then for whatever reason, they backed off. I don't know whether they were thrown off the scent or dissuaded by your lawyers, but you are a doctor. You run a public health agency. Lawyer stuff is for lawyers. We are supposed to take care of people. We are supposed to prevent this stuff from happening, and the system was blinking red for 10 years. So I appreciate that there is a newfound enthusiasm and vigilance after the end of September of 2012. Everything seems to be a pre- and post-meningitis mindset at the FDA and I am grateful for the work that the agency is doing now, but I just fail to understand why you could not do that same work prior to the death of 50 people. It just—it almost defies gravity.

In your own written testimony, you—on the third page, beginning of the top of the page, you actually reference "Since the NECC outbreak", and then you go into magnesium sulfate preparation that was contaminated, apparently with no injuries. Then you talk about eye infections associated with repackaged Avastin. But that is not really new information, because the FDA had received warnings and complaints relating to the sterility of NECC's Avastin products for a long time, 2007. The FDA was repeatedly put on notice that NECC may again be experiencing problems relating to the sterility and/or safety of its products. An adverse drug reaction report which was supplied by you to our committee, so obviously it was received by the FDA, talked about just one of those eye infections that occurred after repackaged, repurposed Avastin—apparently the company took a bulk amount of compound that was duly licensed for treatment of colon cancer, broke it up into smaller amounts, and dispensed it to ophthalmologists for use in treating macular degeneration. The problem is, and as has been referenced by your folks, every time you pierce that vial, the risk for contami-

nation occurs. So you make up multiple preparations that can now be used for intraocular injection, but the last syringes that are prepared that day may have extra stuff in them. You cannot have a preservative to prevent the growth of bacteria or fungus in an Avastin preparation for ophthalmic use, because it is going into the eye and you can't have a preservative injected into the eye.

So I guess what troubles me is you are talking about it here, the serious eye infections with repackaged Avastin, but that wasn't exactly news to you, was it?

Dr. HAMBURG. I think what you are speaking to underscores the fact that we really do now need to recognize that the existing legal authorities and enforcement strategy is not adequate to address the problems that we have. We need to be able to——

Mr. BURGESS. I am sorry, I do need to interrupt——

Dr. HAMBURG [continuing]. Repackaging to sanitary standards.

Mr. BURGESS [continuing]. In the interest of time, because you now are in those companies. I mean, in your own testimony you talk about compounding pharmacies producing what should be sterile products shipping across state lines, and in advance of or without a prescription—I am not a lawyer. I don't really understand what makes a manufacturer a manufacturer, but I feel like that old Supreme Court justice. I don't know the definition of manufacturer, but I know one when I see it, and that is a manufacturer, and you have absolute authority to regulate manufacture of pharmaceuticals, do you not?

Dr. HAMBURG. Yes, we do.

Mr. BURGESS. Yes is the answer. Thank you for the direct answer to that question. And you are doing it now in the post-NECC environment and we are grateful for that enforcement activity. I just got to believe your folks at the various divisions within the agency, I mean, they had to be pulling their hair. In fact, we have the testimony of one of—the fellow that is now the head of the whole New England district office, Mutahar Shamsi, I mean, he said why do we even inspect if we are not going to follow through on these things? They are doing all the work. They are getting right up to the point where, again, someone should pull the plug on the bad guys and they tell the cop to stand down. Don't do it. Your agency must be internally in turmoil because of this.

Dr. HAMBURG. We would very much like to have some of the same kinds of authorities that we have with conventional manufacturers with these highest risk compounders.

Mr. BURGESS. Wait a minute.

Dr. HAMBURG. We do not presently have them, and that is why we are seeking legislation.

Mr. BURGESS. You have the authority to regulate manufacturing. I mean, that is—no one is disputing that. That is not in question. You have that authority. In fact, if you don't believe you have that authority, maybe somebody else ought to run the agency, but you have that authority.

Dr. HAMBURG. Of course we do, but what I am saying to you is we do not have the same authorities to regulate compounding pharmacies.

Mr. BURGESS. If they are manufacturing—if they are engaging in manufacturing, I submit that you do.

Thank you, Mr. Chairman. Maybe we can have time for a second round.

Mr. MURPHY. Thank you. Chair recognizes the gentleman from Michigan, Mr. Dingell.

Mr. DINGELL. Thank you, Mr. Chairman.

I am quite outraged. Here I sit. We are picking nits and straining at nats instead of addressing what this committee should be doing. We should be figuring out what are the problems, and then to proceed to address them. We have had 733 cases, 53 deaths, 15 deaths in Michigan, the highest number of cases, and the deaths, and we are dealing here with an agency that doesn't have the authority to do the things that it needs to do.

Section 503 exempts compounded drugs from three critical requirements at FDA. First of all, they don't have to comply with good manufacturing practices. If you look at what happened up in New England, you will find they weren't even within rock-throwing distance of good manufacturing practices. And so they have no authority to address these things as new drugs. They really have questionable, if any, authority to address these people as manufacturers, and there is no requirement that these things have directions for proper use. In addition to this, these people who have vigorously opposed any kind of control have not only got themselves statutory exemption, but they don't even have to report adverse consequences of the use of their pharmaceuticals.

And here we sit, picking nits about what did Food and Drug know, and when did they know it? This committee should be saying what authority do you need, and then saying by golly, we are going to get it for you.

Now, let me ask you a few questions, Administrator. You said that you don't have sufficient authority to regulate these people. Is that right?

Dr. HAMBURG. Correct.

Mr. DINGELL. Yes. Now, since the fungal meningitis outbreak, FDA has inspected compounding pharmacies that are known to have produced sterile drugs in the past. Is this correct?

Dr. HAMBURG. That is correct.

Mr. DINGELL. Can you explain briefly what the Food and Drug Administration found during these inspections?

Dr. HAMBURG. We have found serious lapses in sterility—procedures, insufficient ventilation——

Mr. DINGELL. I want you to submit that for the record, if you please.

Now, was Food and Drug granted full access to all of the identified compounding pharmacies for inspection? Yes or no?

Dr. HAMBURG. No.

Mr. DINGELL. Would you submit to us what it was that they did to deny you that access?

Now, was Food and Drug granted full access to records by all of the identified compounding pharmacies during inspection?

Dr. HAMBURG. No.

Mr. DINGELL. Did you encounter resistance from any of the identifying compounding pharmacies when Food and Drug arrived for inspection?

Dr. HAMBURG. Questioning of our authority, yes.

Mr. DINGELL. All right. Now, would you please submit for the record what actually happened to you in these cases where they refused you access to the records?

Now, Madam Administrator, even in light of the fungal meningitis outbreak, with 53 deaths and over 700 confirmed cases, some of these compounding pharmacies refused to grant you access to their facility or records for inspection. Yes or no?

Dr. HAMBURG. Yes.

Mr. DINGELL. Do you need inspection authority to effectively regulate compounding pharmacies? Yes or no?

Dr. HAMBURG. Yes, absolutely.

Mr. DINGELL. Do you believe that the states are able or have carried out their responsibilities fully on these matters?

Dr. HAMBURG. It is very variable, but no, not in their entirety.

Mr. DINGELL. OK. Do you believe that FDA has clear authority to access all records when inspecting a compounding pharmacy? Yes or no?

Dr. HAMBURG. I am sorry. Could you repeat that?

Mr. DINGELL. Do you believe that FDA has clear authority to access all records when inspecting a compounding pharmacy? Yes or no?

Dr. HAMBURG. No.

Mr. DINGELL. Has FDA faced litigation regarding its ability to inspect records in pharmacies?

Dr. HAMBURG. Yes, we have.

Mr. DINGELL. Do you need this authority to effectively regulate compounding pharmacies?

Dr. HAMBURG. Yes.

Mr. DINGELL. Would these authorities help FDA to enter a compounding pharmacy without delay to conduct proactive inspections?

Dr. HAMBURG. Yes.

Mr. DINGELL. Would these authorities assist FDA in preventing future outbreaks?

Dr. HAMBURG. Yes.

Mr. DINGELL. Thank you, Commissioner.

Now, I want to make some observations here. This committee has an important responsibility. Our responsibility is to find out if the laws are being properly enforced and if there is additional law that is needed to make the situation better. We are having people who have been killed. We can anticipate if we don't do something more, there are going to be more. The Democratic members on this committee have sent to the leadership of this committee a request to bring in the trade association of these people to discuss what it is they are doing, and why and when and how. They have refused to assist and cooperate with Food and Drug. They have gone further and they have instructed their members as how to obfuscate, delay, and to refuse to comply.

We have a nasty situation on our hands. Let's get down to addressing the problem that is before us. Let's haul the right people in. Let's get the right kind of legislation drafted. Let's get the proper testimony, and let's move forward.

Thank you, Mr. Chairman.

Mr. MURPHY. Thank the gentleman.

By the way, Chairman Dingell has asked for a number of documents for the record, and at the last hearing in November, a number of members also asked for documents. We haven't received those yet, so I would like to expect those documents by the 19th of April, to have answers to those questions.

Dr. HAMBURG. By the 19th of April?

Mr. MURPHY. The questions for the record from the last hearing. the questions for the record from the last hearing, which was in November.

The chair now recognizes for 5 minutes the gentleman from Louisiana, Mr. Scalise, for 5 minutes.

Mr. SCALISE. Thank you, Mr. Chairman. I appreciate you having this hearing and following up on something that we have been delving into for a few months now.

I know I had asked, as others did, back at that last hearing—and I will reiterate, I would like to get whatever law it is that you all are hiding behind that says you do not have the legal authority to investigate these pharmacies like Ameridose and NECC. I don't know why haven't gotten it in the months since our hearing, but can you get us whatever it is that legally you are hiding behind that you say prevented you from doing the proper investigation, things that you are saying you need to change the law now. Well, if you need to change the law now, then clearly you are hiding behind some section of law that you think doesn't allow you to do it today. Can you get us that information?

Dr. HAMBURG. I can certainly get you relevant law. I would just like to underscore that it is not just the FDA that is concerned about the ambiguity in the law. This has been a serious issue for a long time, going back to when it was first enacted, the statute—503A of the Food, Drug and Cosmetic Act, when David Kessler sat before a committee and said that he was concerned that the law was going to create loopholes that would enable compounding pharmacies to be able to——

Mr. SCALISE. But did you just say earlier in your testimony that you have gone and investigated over 50 of these pharmacies since the outbreak?

Dr. HAMBURG. Because we have been able to go in and investigate——

Mr. SCALISE. Well if you have been able to investigate——

Dr. HAMBURG [continuing]. Does not mean that we have the full authority that——

Mr. SCALISE. So you are investigating without legal authority now? Is that what you think you are doing?

Dr. HAMBURG. No, we have the authority to go in, as Congressman Dingell just indicated. We don't have the full authorities we need in order to do the full inspections, and we don't know who they are.

Mr. SCALISE. Well let me just ask you this. We are running low on time, I apologize, but if we can first put up, there is a chart that documents complaints that have been filed for months and months prior to the deaths that you all were receiving. FDA was getting complaints about this facility—not in general, but about this facility. Now, I don't know what you all were doing about it back then, but if you were claiming you didn't have the legal authority to do

it and yet you are getting these complaints, did you at least pick up the phone and call the State of Massachusetts and ask them to use their legal authority to investigate?

Ms. DEGETTE. Mr. Chairman, I have to ask, does the witness have a list of those complaints, because I certainly can't read it from here.

Mr. SCALISE. Do you know about those complaints? I will ask the commissioner. Those complaints, we got them because we got them from the FDA. Do you know that they are out there?

Dr. HAMBURG. I am aware that there were complaints, and——

Mr. SCALISE. So did you all pick up the phone and call the State of Massachusetts?

Dr. HAMBURG. To the best of my understanding, we have made an effort to follow up in the general——

Mr. SCALISE. During the time prior to the 53 deaths, you are getting flooded with complaints from people saying this place is unsafe. It is highly questionable what they are doing. Did you, at some point—when you said in your own decision making process that you didn't think you had the legal authority to go in and check them out, did you at least pick up the phone and say——

Dr. HAMBURG. No. I want to be clear.

Mr. SCALISE. You are here to protect public health. Call Massachusetts.

Dr. HAMBURG. I did not say we don't have authority. We have authority that is not adequate to fully regulate——

Mr. SCALISE. Then why didn't you pick up the phone and call somebody who did? If in your opinion you were concerned about your question on authority, why didn't you call Massachusetts, or did you call Massachusetts prior to the deaths occurring?

Dr. HAMBURG. We——

Mr. SCALISE. That is a yes or no question.

Dr. HAMBURG. We have worked with Massachusetts and we worked with others——

Mr. SCALISE. But did you call the State of Massachusetts and forward the complaints and say look, there is a real serious question about this company in your state. We are not sure if we can go in. You all ought to go in because you have the legal authority. Did you make that call? Did you pass that information on?

Dr. HAMBURG. I have said that——

Mr. SCALISE. Yes or no.

Dr. HAMBURG [continuing]. I do not believe——

Mr. SCALISE. We are running out of time here.

Dr. HAMBURG [continuing]. That our response to the compounding industry and specific issues that you are raising——

Mr. SCALISE. So did you forward any of these complaints?

Dr. HAMBURG [continuing]. Was adequately——

Mr. SCALISE. And this is a yes or no question. Did you forward any of these complaints to the State of Massachusetts prior to the deaths? Any of them?

Dr. HAMBURG. In many instances we are working——

Mr. SCALISE. Yes or no?

Dr. HAMBURG [continuing]. With the states to do inspections.

Mr. SCALISE. Did you forward the complaints? Yes or no?

Dr. HAMBURG. I can't speak to—I don't know what complaints you are referring to, but——

Mr. SCALISE. You don't know?

Dr. HAMBURG [continuing]. In many instances yes, we were——

Mr. SCALISE. Yes, you did?

Dr. HAMBURG. I don't know what complaints you are referring to.

Mr. SCALISE. Did you send the complaints? Yes or no? And I am only trying to pressure—I mean, you were happy to answer Mr. Dingell's questions yes or no. I have got 40 seconds left. Did you forward any of these complaints that you got to the State of Massachusetts? Yes or no?

Dr. HAMBURG. We discussed complaints——

Mr. SCALISE. Yes or no?

Dr. HAMBURG [continuing]. With the states. We did inspections with the states——

Mr. SCALISE. Can you answer this in a yes or no fashion? Are you evading?

Dr. HAMBURG. I can't speak——

Mr. SCALISE. Let me ask you this. I went to your Web site. I went to your Web site. This is right now, live. Your Web site Commissioner's Page says that it is your mission to find "novel ways to prevent illness and promote public health, and be transparent in explaining our decision-making, says Dr. Hamburg." That is you. You are not—number one, you did not find novel ways to protect public health, and you are not right now being transparent in explaining your decision-making process. So you are failing in your mission.

So I will at least ask you this. Maybe you can answer——

Dr. HAMBURG. I am not——

Mr. SCALISE. Has anybody at FDA been held accountable for the 53 deaths that occurred? Anybody?

Dr. HAMBURG. We are working hard, both in responding——

Mr. SCALISE. Has anyone been held accountable? Yes or no? Or do you not know?

Dr. HAMBURG. You know, my statement to you is that we could have been more vigorous, but that——

Mr. SCALISE. Has anyone been held accountable?

Mr. MURPHY. Gentleman's time is expired.

Mr. SCALISE. Have you held anyone accountable? The buck stops with you. You said that today in your testimony. Have you——

Mr. MURPHY. Gentleman's——

Mr. SCALISE [continuing]. Held anyone accountable for 53 deaths?

Dr. HAMBURG. This is a problem that is one that needs to be addressed by——

Mr. SCALISE. I will take that as a no.

Dr. HAMBURG [continuing]. The FDA, states——

Mr. SCALISE. I will take that as a no and I will yield back the balance of my time.

Mr. MURPHY. Gentleman's time is expired. Now recognize the gentlelady from Illinois, Ms. Schakowsky, for 5 minutes.

Ms. SCHAKOWSKY. Thank you, Mr. Chairman, and thank you, Mr. Tonko, for allowing me to go out of turn.

Commissioner Hamburg, by the time the Obama Administration entered office in January of 2009, FDA guidance and law regarding compounding pharmacies had been governed by confusion and uncertainty for nearly 7 years. In May, 2009, top FDA officials met with the acting commissioner, your predecessor, to resolve the issue of unregulated compounding pharmacies. I want to ask you about a document that the FDA produced—gave to the committee. You can find it at Tab 45. It is a written summary of a meeting that occurred on May 12, 2009. This summary of the meeting noted that "Unregulated compounding raises significant public health concerns. FDA has seen numerous examples of serious patient injury and death caused by improper compounding." At this meeting, the recommended path forward was to seek legislation amending Section 503A to enhance FDA's oversight of compounded drug, much, I guess, like you are saying now to do that.

But this document also lists a disadvantage of that legislative approach, and the summary stated "The legislative process will be time and resource intensive, and the compounding community will actively oppose the changes that we seek. They have a very effective grass roots organization that will make it difficult for us to achieve our legislative ends. We cannot know if the result of our efforts will be better law than Section 503A in its current form."

So Dr. Hamburg, this was not a meeting that you attended, and I am not going to ask you about it specifically, but I would like to ask you a question about the influence of the compounding industry generally, and its leading trade group, the International Academy of Compounding Pharmacies, or IACP. Can you describe the general views of the compounding industry with regard to the FDA authority that you are talking about requesting today?

Dr. HAMBURG. Well, I think it is clear that the organization and the industry more broadly has, over many years, questioned our authorities to fully regulate the compounding pharmacies. They have challenged us in court, as has been documented, and in addition to questioning FDA authorities, as was demonstrated in the document that was put together by Congressman Waxman and others, they also were making concerted efforts to weaken regulatory authorities at the state level and I think that this was even while recognizing that this could lead to some serious concerns, and certainly it has made our ability to regulate this industry much more challenging. It has required much more complexity in terms of the actions we can take and the resources required to take those actions, and it has certainly also thwarted earlier efforts at legislation. In 2007, Senators Kennedy, Burr, and Roberts proposed some legislation that would have strengthened the FDA role and clarified some of these issues, and industry was up on the Hill lobbying intensively, and that legislation was never introduced. And I don't believe there was anything on the House side either.

Ms. SCHAKOWSKY. So would you say that the IACP has made it more difficult for FDA to effectively regulate drug compounders?

Dr. HAMBURG. I would.

Ms. SCHAKOWSKY. And would you agree that the compounders have traditionally been adamantly opposed to any expansion of FDA authority over drug compounders?

Dr. HAMBURG. Absolutely, and I think the industry is questioning the inspections that we are doing now.

Ms. SCHAKOWSKY. So Dr. Hamburg, earlier this week the subcommittee released a letter asking that a representative of compounding pharmacies be invited here today, but the Majority rejected our request. I would like to ask that the letter and underlying documents, all of which show that the compounding industry has fought relentlessly to avoid FDA oversight, be added to the hearing record.

Mr. MURPHY. Without objection.

[The information appears at the conclusion of the hearing.]

Ms. SCHAKOWSKY. Thank you.

I think this proceeding would have benefitted from hearing their testimony. Our drug supply needs to have FDA oversight and drug compounders shouldn't get to create—to evade regulation by the agency. We as a committee need to join together and finally give the FDA, give you the authority that you need, that the agency needs to effectively oversee drug compounders.

And I yield back.

Mr. MURPHY. The gentlelady yields back. I now recognize Mr. Olson for 5 minutes.

Mr. OLSON. I thank the chair, and welcome, Dr. Hamburg.

As you know, ma'am, one of my duties as an elected representative of the people of Texas 22 is to provide oversight and investigate the Executive Branch to ensure that they comply with the Constitution and the laws. Put simply, my job is to find the truth. The truth is that 55 Americans died because their spinal injection was contaminated, and at least 700 Americans were made seriously ill by that drug. These families deserve to know the truth, and I intend to get that for them.

During your testimony in November, you made a number of statements about how the compounding industry has evolved in recent years. You also highlighted that the Massachusetts State Pharmacy Board was in the best position to oversee NECC. But that decision was made in 2003, is that correct?

Dr. HAMBURG. As I think you probably know, compounding pharmacies historically have been regulated by states, and it is the states that license pharmacies.

Mr. OLSON. Yes, ma'am. These are complaints—please refer to Tabs 2 and 3 in your binder there. I will give you some time to do that. These complaints about the NECC from pharmacists in Wisconsin and Iowa that the Massachusetts Pharmacy Board forwarded to FDA in April and May of 2004.

In an e-mail to Massachusetts Board related to the second complaint in Tab 3, the lead attorney for the board asked, could you clarify what we may not have known about your operation previously that this e-mail tells us, as in what the FDA might not know in a prior assessment that the NECC was not a "manufacturer."

Commissioner Hamburg, a different picture of the NECC began to emerge soon after the FDA decided the state should take the lead, isn't that right? Much different picture, ma'am, much different.

Dr. HAMBURG. As I think was discussed at the last hearing, it was agreed during this early period that, in fact, the State of Massachusetts had the lead in responding because it was a licensed pharmacy in Massachusetts. However, I think it is important to underscore that the line between compounder and manufacturer is not a bright one, and that that is part of what we are seeking is to get more explicitness in law with respect to what is a manufacturer and what is a compounder.

Mr. OLSON. Yes, ma'am, but these documents show that by 2004, soon after the FDA's decision that the state would take the lead in overseeing NECC, FDA had already begun to receive information showing that the company was shipping products across the country without patient-specific prescriptions. Based on documents provided, pharmacists and hospitals continued to forward NECC's solicitation to you, to the FDA.

Let me give you one example. It is Tab 4 there in your binder. In January of 2006, the FDA received a complaint about NECC soliciting a multiple use sterile injectable product. Are you familiar with this complaint, ma'am? Yes or no?

Dr. HAMBURG. Yes.

Mr. OLSON. Yes. This complaint stated that NECC does, and this is a quote, "not need or desire to have the patient's name." This would suggest that the company is no longer acting like a compounder, right? It is not filling patient-specific prescriptions.

Recently, a 60 Minutes report in which you were interviewed, an NECC anonymous informant claimed the company was forging patient prescriptions. Are you familiar with that charge, ma'am? Yes or no?

Dr. HAMBURG. You know, with respect to some of these specific documents, et cetera, because of the ongoing criminal investigation—I discussed this with the chairman before—I cannot characterize this situation for you. We all want that criminal investigation to go forward, and I do not want to——

Mr. OLSON. Ma'am, with all due respect——

Dr. HAMBURG [continuing]. Do or say something that would compromise that.

Mr. OLSON [continuing]. You are not the subject of an open investigation. This committee has not sought any documents from the FDA or U.S. Attorney's Office that are being used in an open criminal case. By definition, we are not asking any questions about the open case or evidence that is part of that case. This Congress does not necessarily have your respect for "open criminal case" and that excuse. Thirty years ago in the Reagan Administration, this committee and other committees in the House held EPA Administrator Anne Gorsuch in contempt for not producing documents, even though Administrator Gorsuch was advised by Department of Justice and the White House that she could not produce to Congress these documents because of executive privilege. Please give us these documents.

Again, I don't think open case applies. It hasn't historically. It shouldn't apply here.

Dr. HAMBURG. You clearly have a huge number of documents, but I cannot speak to the specifics of some of these documents because of the ongoing criminal investigation. I don't know the spe-

cifics of what is—I am not part of the ongoing criminal investigation in terms of the collection of information and its analysis, but I have been told that I need to be careful not to compromise that investigation.

Mr. OLSON. That is——

Mr. MURPHY. Gentleman's time is expired.

Mr. OLSON [continuing]. A subject of investigation and we have not sought any documents from FDA or——

Ms. DEGETTE. Mr. Chairman?

Mr. MURPHY. Gentleman's time is expired.

Mr. OLSON. I yield back.

Ms. DEGETTE. I would respectfully ask that members—I would ask unanimous consent to ask Commissioner Hamburg, were you advised by counsel not to answer questions about the ongoing criminal investigation at NECC?

Dr. HAMBURG. I was.

Ms. DEGETTE. So Mr. Chairman, I would ask members not to ask those—if she has been advised by counsel not to do that, I don't want to hurt a criminal investigation of a company that has killed 55 people and sickened hundreds more, and I am going to assume no one else does.

Mr. MURPHY. I am assuming you would be able to show us a letter from the Attorney General or someone's office saying you cannot speak to certain subjects here so we know exactly where you can and cannot. Can you show us some documentation?

Dr. HAMBURG. Well, I don't have such a letter but I was advised that I should be very careful about not compromising the criminal investigation, and I think we all share that concern. None of us want to imperil the important criminal investigation that is ongoing.

Mr. MURPHY. I appreciate that. We will make sure we ask questions relevant to what you did and didn't do, and what the FDA is responsible for in this. Thank you.

Chair now recognizes the gentleman from New York, Mr. Tonko, for 5 minutes.

Mr. TONKO. Thank you very much, chair.

First, thank you for appearing before the committee, Dr. Hamburg, and thank you for your service as commissioner at FDA.

It has been well-documented that the FDA has been stepping up its inspections of compounding pharmacies in the wake of tragedies, and while that is a first good step, can you tell us which additional efforts you need? What follow-up intervention would and should be available as the next tools in the kit to do your job and do it effectively?

Dr. HAMBURG. Well thank you for that question. We do feel that we want to be more aggressive, and to do that, there are some critical gaps in our authorities.

First of all, we need these companies that are making the highest risk products, the sterile products, in advance of or without a prescription and shipping them interstate, they need to be held to a national uniform standard for safety practice in good manufacturing that they will adhere to, that we can inspect against, and that we can take enforcement actions against that will hold. They need to be required to register with us so that we can even know

who is out there and what they are making. And we certainly want them also to report adverse events to us if they hear about them in relation to a product so that we can get in quickly and try to mitigate that problem as fast as possible.

Mr. TONKO. Thank you. The partnership, the interrelationship with the state authorities, are there requirements for them to inform the FDA as to findings? Does the ball rest in your court to approach them? Are they required—is there a registry of sorts that requires them to update you routinely as that structure—is it standardized?

Dr. HAMBURG. A very important question. As you know, states historically have regulated compounding pharmacies, as they do the practice of pharmacy in general, and states have very different laws with different requirements. But as far as I know, there are not any specific requirements on reporting to the FDA. We often work in concert with states and that is important, and we sometimes piggy-back on their authorities when we are going into facilities and, for example, trying to get access to records which we might be denied. Going forward, we feel very strongly that we need to strengthen the working relationships with the state and systematize some of the mechanisms for communication, because that will make a difference.

In these recent inspections that we have just done, we did do them in almost all the cases in coordination with the states.

Mr. TONKO. It seems to me that there was a lot of talk as to what intervention there was or what interaction there might have been between FDA and the states. It seems to me there is an added safety net offered if there is a structured, standardized requirement of states to inform good and bad news being shared with you about their oversight and to give an authority that they now have. I think that would improve the system.

And also, you asked about the explicitness of some of the details that guide your day-to-day operations in these matters. Are there other things you would bring to this committee's attention that would be useful and provide for, perhaps, more public safety here and consumer protection?

Dr. HAMBURG. Well, I think what is just abundantly clear and is demonstrated in the documents that we have given to you is that we have been compromised in our ability to provide the full and aggressive enforcement that I think is necessary to protect the health of the American people, that we have an ambiguous statute. We have a statute that is complicated by differing court opinions that reflect the ambiguity that even federal courts can't agree about what the law is and how it should be applied. And that just is not a system that serves anyone, and that is overlaid on the fact that all of the states have different laws and practices. So we do not have the kind of strong regulatory system that really can assure safety and get patients the products that they need.

In addition, the statute doesn't fit the current healthcare environment, patient needs, hospital needs. It is simply the wrong fit and we have an opportunity—I think we have an obligation now to work with all of you to try to make sure that we have the kind of regulatory program in place, the kinds of laws that we can really build on and enforce against.

Mr. TONKO. I appreciate that effort, and I would hope that we gather this information and go forward and do the work that is essential to respond to—in the aftermath of these tragedies to the needs of the general public.

So thank you again for your information here today.

Dr. HAMBURG. Thank you.

Mr. MURPHY. Right now recognize the——

Mr. TONKO. I yield back.

Mr. MURPHY. Gentleman yields back. We now recognize for 5 minutes the gentleman from Virginia, Mr. Griffith, for 5 minutes.

Mr. GRIFFITH. Dr. Hamburg, while the circuits may disagree on some aspects of the law, isn't it correct that in order to be a compounding pharmacy, you are supposed to be making something for a specific patient with a specific prescription? Isn't that true?

Dr. HAMBURG. Well in fact——

Mr. GRIFFITH. Yes or no?

Dr. HAMBURG [continuing]. Many states allow anticipatory compounding and——

Mr. GRIFFITH. I am talking about the code that—the Federal Code, and isn't it true that for federal purposes, it is supposed to be a specific prescription and a specific patient? Yes?

Dr. HAMBURG. That is.

Mr. GRIFFITH. All right. Now let's move on to the sister of—the sister company of NECC, Ameridose, because they also had problems and you all received—FDA received information about those problems at Ameridose in 2009, 2010, 2011 from internal company sources, isn't that correct? Yes or no?

Dr. HAMBURG. That is correct.

Mr. GRIFFITH. And the concerns that were raised related to the safety of the products and practices at Ameridose, but also the company's management, isn't that also correct?

Dr. HAMBURG. Yes.

Mr. GRIFFITH. And isn't it correct that you all were alerted by the folks in Ohio that there was actually a question that they didn't have these prescriptions for individual patients, but in fact, were manufacturers and Ohio was asking you all to look into this in trying to decide whether they were going to issue a Cease and Desist letter? Isn't that also correct?

Dr. HAMBURG. Again, I apologize but we are getting into the area of an ongoing investigation and——

Mr. GRIFFITH. I am asking you if it is a fact whether you gave information to this committee, and I want it out there in the public so everybody in the United States knows, you all received information—I am not asking you whether it was true or not, but you received information from the State of Ohio that they felt like what they were looking at with Ameridose was a manufacturer and not a prescriber. Isn't that correct? Excuse me, not a compounder, because they didn't have specific prescriptions. You received that information, yes or no?

Dr. HAMBURG. You know, I actually cannot speak to that specific document.

Mr. GRIFFITH. So you were unaware that this information had come to the attention of the FDA that Ohio was very concerned about this?

All right, I am going to move on. Are you aware that there were notes that were involved in these complaints and concerns about whether or not there was going to be an investigation, and that one of those notes—and I would point you to Tab 26, go to the second part where it starts listing out things, and it says—I believe I have got this right here. On page 4, note 4, specifically part of the inspection was to read "Are written prescriptions/physician orders for identified individual patients received before dispensing compounded injectable products each time they are dispensed?" That is part of one of your own memos, is it not?

And Mr. Taylor, if you want to jump in here, it might be your memo, but it is an FDA memo. Yes or no?

Dr. HAMBURG. The issue about prescriptions is one that has been an area of ambiguity in terms of whether 503A applies or not, et cetera, and it has been part of this changing landscape in terms of——

Mr. GRIFFITH. There was an inspection request and as a part of that inspection request, attached to that was background information and what you ought to do, and one of those was to look into that information. But you all never did that with Ameridose, did you? Before the NECC problem, their sister company was discovered through the deaths of American citizens and 1,415 people in my region of the State of Virginia and a little bit over into West Virginia were impacted by these drug companies or these manufacturers posing as compounders. You never asked for that information—the FDA never did that, did they?

Dr. HAMBURG. As I said, there is an ongoing investigation by the FDA with respect to Ameridose, and we are——

Mr. GRIFFITH. All right. You never held an inspection, yes?

Dr. HAMBURG. We have inspected Ameridose on a number of occasions, but I cannot speak to the specifics.

Mr. GRIFFITH. All right. And there were numerous requests to inspect both Ameridose and NECC, and as these inspection requests came in, you all sometimes—you answered earlier that to get a warrant might take you days or weeks, but isn't it true that on several occasions when NECC wrote you back and said we don't think you have authority, you took 2 years before you even sent them a letter back? Isn't that not also true?

Dr. HAMBURG. As I said, I wish that we had been more prompt——

Mr. GRIFFITH. And I appreciate that, and I do appreciate the answers today much better. My time is running out, ma'am, so I am going to move on. I do appreciate it. I understand that you are now going to be more aggressive, but in order to fix this, we have to figure out where the problems are. And when you have 2-year delays when somebody just sends you a letter and says hey, we don't think you have authority, that is not acceptable. I believe that we have got to figure out what the problems were, not just at NECC, but across the board. I believe there are a lot of companies out there posing, perhaps, as compounders who are really manufacturers and I think if you insisted on the requirement that there be a prescription for a specific patient or that the compounding made for a specific patient like it was for my son on one occasion, then we

wouldn't have had this problem in the first place and I think you all failed the American people.

Mr. MURPHY. Gentleman yields back. Now recognize the gentleman from Texas, Mr. Green, for 5 minutes.

Mr. GREEN. Thank you, Mr. Chairman. Again, thank you, Dr. Hamburg, for coming back. I remember the hearing that we had earlier, and I have to admit, having been on the committee for a long time, I didn't think the FDA was something we could be proud of then because of what my colleagues on the other side have talked about.

Since the fungal meningitis outbreak was traced back to the so-called compounding pharmacy in Massachusetts, all we have seen is finger pointing from the FDA, the industry, Republicans, Democrats, even states have played this role, and it is time for the finger pointing to end and we begin to legislate.

I have always supported community-based compounding pharmacies, because historically that is how pharmacies started. But I was shocked at what was going on in Massachusetts was considered the same type of facility as my neighborhood compounder who is filling the prescription from a physician, or even a larger pharmacy that supplies hospitals or large practices, or even a heavy client load. And to know the FDA is requesting additional authority from Congress to regulate certain compounding pharmacies.

I also know that that was your testimony previously, but in the meantime, you have been able to open up investigations. So you can see why from our side of this, it looks like maybe FDA did have some authority and just didn't use it. But I also know that in a legal situation, you probably need some background or some support based on changing the law. But I don't want you not doing what you are doing right now, and I know you have opened some investigations. So somewhere along the way, one of your attorneys said we can do this now. And I guess they didn't tell you that 2 years ago or whenever. Is that correct?

Dr. HAMBURG. I want to be clear that I never said we didn't have authorities. I said our authorities were limited and we are determined to be as aggressive as possible using our current authorities. But they are not adequate to provide the American people with the safety protections that they need, and our current round of inspections are, I think, underscoring that fact that we cannot have an inspectional system in a regulatory regime where the very players that are at the center of the questions don't even have to register with us, don't even have to let us know what——

Mr. GREEN. And I agree, but what the FDA is requesting the authority, is it over all compounders, including the ones who are regulated by the states, particularly like a local compounding pharmacist who just does prescriptions? Does the FDA want to get into that, or do you want to look at the manufacturing that only goes across state lines?

Dr. HAMBURG. Traditional compounding, the corner pharmacy type you are describing, I think has a very important role in our healthcare system, and we all recognize that. We are concerned about this evolving new hybrid of compounding pharmacy that is making sterile, high risk products in advance of or without a prescription and selling across state lines. We do believe we need new

authorities in order to adequately regulate them. Again, they provide an important service to our healthcare system. Hospitals depend on the products that they make, and if done right, they can make these products safe.

Mr. GREEN. That is one of my concerns, and I am going to run out of time, and you know our time limits.

As we write legislation, we should keep in mind that your intent is to try to keep the compounding pharmacies that are locally in the domain of state regulators, but for example, in Texas we have a great medical center in Houston, and I am assuming they have a contract with some type of compounding company that—whether it is across state lines or not, that they may work with, but that compounding company is using prescriptions from this medical center or this hospital system or this practice of doctors. You don't intend to go as far as for someone that has a prescription from either a group of doctors to a compounding pharmacist?

Dr. HAMBURG. We appreciate the tradition and the importance of traditional compounding. We do think that there are some requirements that should apply to all compounders, big or small, traditional, non-traditional. For example, there are certain products that probably should not be compounded by pharmacies, no matter what. They should be made by manufacturers within the new drug approval process to assure safety and efficacy, products that are complex and involve hard-to-deliver kinds of mechanisms, et cetera. We also believe that FDA-approved commercially available drugs should not be——

Mr. GREEN. OK. I hate to cut you off, but I want to ask—get a chance to ask you a question. These additional inspections that you are doing now, or the additional authority, does FDA have the capacity to expand on that, considering the funding flow that you already have? Are you going to be able to find the money to do that, even if Congress continues with sequestration, which it looks like we are, but also with the current appropriations process?

Dr. HAMBURG. It is an enormous concern in terms of the expansion of responsibilities. Already, we are responsible for overseeing some 5,600 conventional manufacturers. It is estimated there are about 28,000 compounding pharmacies overall, probably 7,500 or so specialty pharmacies, and about 3,000 that are doing sterile compounding.

Mr. GREEN. Mr. Chairman, I am out of time and I understand. I have one more question I would like to submit, if we could submit a question particularly dealing with the Texas—an entity in Texas with—but I would like to submit that too if I have permission to do that.

Mr. MURPHY. Yes, and we probably are going to be doing a second round, too. If you are still here, you can ask that directly.

Mr. GREEN. OK. If we do a second round, I will be back.

Dr. HAMBURG. OK.

Mr. MURPHY. Now recognize the gentleman from Ohio, Mr. Johnson, for 5 minutes.

Mr. JOHNSON. Thank you, Mr. Chairman.

Ms. Hamburg, you said in a response to our colleague, Mr. Tonko, a little while ago that you want compounding pharmacies to report adverse events so we can mitigate them as fast as pos-

sible. Would you please explain briefly, what is an adverse event report?

Dr. HAMBURG. An adverse event report is when someone submits to the FDA a concern about a product. It doesn't mean that actually there is a legitimate or ultimately verified concern, but it is that there seems to have been some negative reaction associated with a product.

Mr. JOHNSON. OK. Well the FDA made a decision in 2011 to suspend inspections of compounding pharmacies until the agency could issue guidance on compounding and manufacturing, right? That is what you have testified to thus far?

Dr. HAMBURG. Yes.

Mr. JOHNSON. That is a yes, correct?

Dr. HAMBURG. Yes. You know, it is a bit more complicated than that——

Mr. JOHNSON. No, it was a very simple question. The FDA made a decision in 2011 to suspend inspections of compounding pharmacies until the agency could issue guidance on compounding and manufacturing.

Dr. HAMBURG. We were doing for-cause inspections when we learned about a problem——

Mr. JOHNSON. Well, I want to talk about certain adverse event reports that came into the agency about Ameridose after this decision to suspend inspections were made. The agency produced these reports to us, but didn't produce any documents showing how the agency responded to them, so let me run through them.

They are located—the complaints are located in your binder starting at Tab 40. We know that the FDA didn't conduct any inspections of Ameridose from 2011 until the outbreak. Is that accurate? Is that correct?

Dr. HAMBURG. After 2011, I do not believe we did any inspections.

Mr. JOHNSON. OK. I want to determine what the FDA did with these reports, including sharing the information with the state or investigating them. On November 17, 2011, FDA received an adverse event report associated with three pregnant women in labor having to have c-sections, since the epidural injections of an Ameridose-made Fentanyl product were not working. Did the FDA take any action on that adverse event report?

Dr. HAMBURG. My understanding is that we were in there inspecting. We did——

Mr. JOHNSON. No, I am not asking if you were in there inspecting. I asked did the FDA take any action on that adverse event report? You testified earlier that you want to mitigate them as fast as possible, so these have a sense of urgency to them in your own opinion. Did the FDA take any action on that report that came in on November 17?

Dr. HAMBURG. I can't speak to every complaint——

Mr. JOHNSON. Would you get that back to the record?

Dr. HAMBURG. I will get back to you on that.

Mr. JOHNSON. OK. On January 24, 2012, FDA received an adverse event report associated with Ameridose-made Fentanyl injections. This time, the complaint related to confusing labeling resulting in two near-misses where nurses had stated that they almost

gave their patients 100 milligrams instead of 50 milligrams. What action did the FDA take in that case?

Dr. HAMBURG. I would like to get back to you on that.

Mr. JOHNSON. OK, submit that one for the record as well, please. Can I have your commitment on that to submit that one to the record?

Dr. HAMBURG. Yes.

Mr. JOHNSON. OK. The next day, on January 25, 2012, FDA received an adverse event report involving an Ameridose-made Heparin-IV bags that a hospital administered to patients, only for the hospital staff to determine after several tests that the bags contained no Heparin. What did the FDA respond to that adverse event report?

Dr. HAMBURG. Again, it would be very helpful to me, because of the ongoing FDA investigation——

Mr. JOHNSON. They are in your tab, ma'am.

Dr. HAMBURG. I am uncertain what would be harmful for me to say——

Mr. JOHNSON. No, what did the FDA do in response to that adverse event report, if anything?

Dr. HAMBURG. You know——

Mr. JOHNSON. Get that back for the record, also.

Dr. HAMBURG [continuing]. Adverse event report——

Mr. JOHNSON. Looks like we are striking out here. My time is limited, ma'am, because I have several others here. On March 12, 2012, the FDA received another adverse event report involving potency issues with Ameridose-made Fentanyl products, at Tab 43. Any response by the FDA?

Dr. HAMBURG. I would like to get back to you——

Mr. JOHNSON. OK, I would appreciate that.

Dr. HAMBURG [continuing]. Because I can't respond to——

Mr. JOHNSON. Less than 2 weeks later, on March 23, 2012, the FDA received yet another report involving another hospital close call associated with confusing Ameridose labeling. That is at Tab 44. I am out of time, so I will ask you to get me responses back—the committee responses back on all of those, please.

Mr. MURPHY. Gentleman yields back. Chair now recognizes Mr. Long of Missouri for 5 minutes.

Mr. LONG. Thank you, Mr. Chairman, and thank you, Dr. Hamburg, for being here today. I know this hasn't been real easy, and Mr. Taylor, for your assistance.

The President stepped to the microphone yesterday and said that at a time like this with the Boston attack yesterday, that we are not Democrats and we are not Republicans, we are Americans. And I think when a situation like this NECC situation with the FDA comes up, well, that is how we need to approach things, as Americans, and trying to get to the bottom of this and see what you can do to be helpful to us and what we can to do be helpful to you. Back in—do you remember the first time—when was the first time you were apprised of the fact that warning signals or warning flags had been raised about the activities of the New England Compounding Center?

Dr. HAMBURG. You know, as I think I said before, as Commissioner, I am not aware of every enforcement action that is being

taken, every complaint that comes in, and so, unfortunately I was not aware of many of the facts that are now before us until——

Mr. LONG. Well, I am just asking the first time that you——

Dr. HAMBURG [continuing]. This tragedy occurred.

Mr. LONG. The first time you were apprised of this, I mean, was it on a newscast, or how were you made aware of the serious problem?

Dr. HAMBURG. You know, I became aware of NECC when the first reports of the meningitis outbreak began to emerge, and you know——

Mr. LONG. Which was approximately——

Dr. HAMBURG. Which was in the fall of 2012, and we began to work very quickly with our colleagues at the state level, and with the CDC to try to understand the nature of the contamination and what could be done to address it, and to make sure that appropriate actions were taken.

Mr. LONG. Prior to that time, had you all ever inspected the facilities of NECC? Had the FDA ever been in there and done any inspections?

Dr. HAMBURG. Yes, there had been inspections.

Mr. LONG. What type of inspection? I mean, what were they inspecting for? I mean, is this something where you would monitor for such things as mold, or do you do microscopic tests, or what kind of inspections would you conduct?

Dr. HAMBURG. Well, I think we were not doing routine inspections because NECC was being regulated by the State of Massachusetts as a licensed pharmacy. But over the course of history, we were in there for various reasons in response to specific complaints of product contamination or adulteration or misbranding.

Mr. LONG. Did you know they were bad actors then? I mean, would you have considered them a bad actor from your prior experience?

Dr. HAMBURG. This is the area that I cannot address because of the ongoing criminal investigation.

Mr. LONG. But you have no letter or anything from Justice or anyone telling you not to speak here openly today about—to answer a question, I guess?

Dr. HAMBURG. You know, I think none of us would want to compromise the importance of that criminal investigation and what——

Mr. LONG. We don't want to compromise the American public, either, and——

Dr. HAMBURG. No, and that——

Mr. LONG. We have had 53 deaths and we have 700 and some that are ill now with it, might lead to their demise. There is another—I think Morgan Griffith said there are 1,400 and some just in his district alone, so—but back on April—in fact, it has been 2 years and 1 day ago, Colorado issued a Cease and Desist order to the New England Compounding Company, or whatever the last "C" is on there, for shipping drugs to states without requiring individual prescriptions for each drug. Back then, 2 years ago, prior to 2012 and this outbreak, what—isn't there somewhere you all called off the dogs for a year? What point was that?

Dr. HAMBURG. Well, I think you are referring to a Cease and Desist order that had happened——

Mr. LONG. From Colorado.

Dr. HAMBURG [continuing]. Based on Colorado State pharmacy law.

Mr. LONG. Right, but that didn't raise any red flags to you all that——

Dr. HAMBURG. You know, as we have discussed, states have very different laws with respect to what they will allow in their states, and what also they will license pharmacists and pharmacies to do, and we did do that as a matter of state law fundamentally.

Mr. LONG. You said earlier in your testimony that we needed legislation, and legislation takes a little while in this town. And while we are waiting for this legislation, what are you doing in the interim to prevent this from happening again, or continuing to happen? There may be other compounding facilities out there as we speak with mold in their facility, along with other things. What are you doing now?

Dr. HAMBURG. Well, I am deeply concerned that we could have another tragedy, and that is why I really am hoping we will be able to work with you on new legislation. But in the meantime, we are going to apply our current authorities as adequately as we can, recognizing that they are limited, that they don't allow us to know everyone who is out there and what they are making. They don't allow us to have a clear uniform set of standards that are enforceable in law for these highest risk compounders to adhere to, and that we are being challenged every day about our authorities in terms of the industry believing that we are overstepping, that we don't have authorities, and we know we need changes in the law in order to really be able to proactively provide the kind of regulatory framework that will prevent problems from happening in the first place, rather than responding——

Mr. LONG. Short of having new legislation, are you satisfied that your agency is doing everything possible——

Mr. MURPHY. Gentleman's time is expired.

Mr. LONG [continuing]. Now to protect the American public in the interim? Because like I said, it takes forever and a day to get new legislation done in this town.

Mr. MURPHY. Gentleman's time——

Dr. HAMBURG. Yes.

Mr. LONG. Particularly when one side of the aisle refers to the other side of the aisle, and then that side of the aisle refers to their friends on the other side of the aisle. Like I said, I want to go back to my opening statement that I think we need to all work as Americans for a solution here and forget this malarkey about each side of the aisle. I think this is one time that we need to pull together, because there has been a lot of people that—families that have been crushed by this and——

Mr. MURPHY. Gentleman's time is expired.

Mr. LONG [continuing]. We need to prevent this in the future. I yield back what time I don't have.

Mr. MURPHY. Thank you. Gentleman's time has expired. Now recognize the gentlewoman from North Carolina, Ms. Ellmers, for 5 minutes.

Mrs. ELLMERS. Thank you, Mr. Chairman, and thank you, Dr. Hamburg, for coming today. I do have many questions, but most importantly, I would like to say that I am incredibly confused by your testimony, and because I am confused, I would like to try to break this down into very simple terms. I would like for you to answer as if you were answering to one of the 53 families who are now without their loved one as a result of these actions that have taken place.

You continuously contradict yourself on what the FDA knew, what the FDA did not know, what the FDA passed on to the state, what the FDA did not pass on to the state, and then when you find yourself in a corner, you say that you cannot respond because of the ongoing criminal investigations. So let's try to get to the bottom of it in very simple terms, because there again, one minute you were going in for inspections, and then the next minute you were not going in for inspections. One minute you understand that there were complaints filed, and the next moment you did not know that there were complaints filed. I don't understand how we can get to the bottom of this situation. Furthermore, I would like to say that I don't understand how more legislation, regulation, and authority is going to help this situation, when the FDA did not apply what they already had. That is very confusing to me because the authority that was there, the authority that you had to share information with a state obviously did not take place. Were there complaints that the FDA received shared with the state? Yes or no?

Dr. HAMBURG. In some cases, but what you asked me to speak to the families——

Mrs. ELLMERS. There are a number of incidents of complaints there starting in 2002 all the way to 2012. Which of those complaints were shared with the state? Now mind you, I understand in your testimony you said here that you worked very quickly with your colleagues at the state level. How did you work with the state level when this went on for 10 years?

Dr. HAMBURG. You know, I think the critical point that I want to make to you and would make to the families and their victims is that I wish that the FDA had been more aggressive——

Mrs. ELLMERS. That is the third time you have used the term "I wish." I bet that those families wish you had acted as well.

Now let me go on to my questioning, because again, I am so confused as to what authority you have, what authority you don't have, how you have worked with the states, because they are the licensure of these pharmacies and compounding pharmacies/manufacturers. You know, we keep getting into this gray area and that seems to be your reasoning for inaction.

I have some documentation in front of me, some from the previous hearing that took place, of which I was not here. I am a new member to the Energy and Commerce Committee. Basically you said at the last hearing in your written statement, you pointed to the fact that the state had inspected NECC in 2011 and found that the facility to be "satisfactory." Commissioner Hamburg, when did FDA first become aware of the inspection by Massachusetts Board of Pharmacy that had taken place? Did you know about this?

Dr. HAMBURG. I was not aware of it personally until preparing for the hearing, but——

Mrs. ELLMERS. So it was——

Dr. HAMBURG [continuing]. Let me say that it is not surprising that you are confused, because even federal judges have been confused about——

Mrs. ELLMERS. We are not going to talk about federal judges today. We are going to talk about the FDA. We are going to talk about your role and your responsibility. Was it in preparation—that inspection, was it in preparation for the November hearing?

Dr. HAMBURG. Was it preparation, yes.

Mrs. ELLMERS. OK. Did you know that the state's inspection you cited was announced and conducted solely in connection with the renovation of NECC, and that inspection had taken place not as a follow-up to previous violations, or the complaints, but because they were actually under renovation?

Dr. HAMBURG. My understanding that—this is really a question for the state—that as part of their licensure as a compounding pharmacy in Massachusetts, they needed to have the state come in to do an inspection when they were——

Mrs. ELLMERS. And they said that they were satisfactory?

Dr. HAMBURG [continuing]. And that was where they were—and I think that was the facility where subsequently these products were being made.

Mrs. ELLMERS. And it was called satisfactory?

Dr. HAMBURG. It was a state inspection, but that is my understanding.

Mrs. ELLMERS. OK. All right, I am looking forward to the second round of questioning. Thank you.

Mr. MURPHY. Thank you. Now recognize Mr. Harper for 5 minutes.

Mr. HARPER. Thank you, Mr. Chairman.

As you are likely aware, CMS recently modified its billing methodology for compounding pharmacies providing drugs used in implanted pain pumps. This change jeopardizes access to necessary pain medications for some of Medicare's most vulnerable beneficiaries. Even more, this change prohibiting compounding pharmacies from billing Medicare directly eliminates an important accreditation requirement designed to protect patient safety. Pharmacies billing Medicare directly for these drugs must comply with Medicare, supplier standards, and federal regulations such as U.S. Pharmacopeia 797. These standards provide an additional layer of quality promotion and patient safety for compounding pharmacies and dispensing sterile products for use in implanted pain pumps.

On the other hand, pharmacies which sell their compounded products to physicians, clinics, or hospitals are not required to be accredited, since they do not bill Medicare directly. In light of the recent tragedy relating to a pharmacy which appears to have been acting outside of its licensure, I believe it is critical that CMS and FDA encourage models of care that promote patient safety.

Saying this, do you find it concerning that CMS in the wake of a tragic outbreak is encouraging pharmacies to sell drugs directly to physicians, as opposed to billing Medicare directly and complying with quality accreditation standards?

Dr. HAMBURG. You know, I am really not an expert on the CMS policy in this regard, and so I think—I mean, many aspects of your

question are probably best directed toward CMS, but with respect to the FDA role, I would like to be able to look at the question you have asked and get back to you.

Mr. HARPER. Would you be willing to look into that situation and if you are indeed concerned about that, would you be willing to express your concern to CMS about that?

Dr. HAMBURG. Yes.

Mr. HARPER. OK. In September, 2008, the head of the FDA New England office, Mr. Shamsi, e-mailed a senior FDA compliance officer, Ms. Autor, and asked to do a new inspection of NECC due to concerns about sterile injectables. Now, sterile injectables are difficult drugs to make, am I correct?

Dr. HAMBURG. That is correct.

Mr. HARPER. Some have questioned whether compounding pharmacies should even make these drugs, am I correct?

Dr. HAMBURG. Some have, yes.

Mr. HARPER. At the time the request for a new inspection was made, the 2006 warning letter was still pending because FDA hadn't replied to NECC's response to the warning letter. I would ask if you would refer in your notebook to Tab 19, if you could look at that? Tab 19. In this e-mail from October 1, 2008, Mr. Shamsi, the current head of the FDA district office, e-mailed Ms. Autor, a senior compliance officer, and asked whether "our lack of response would hinder any further action against NECC?" Mr. Shamsi believed the FDA lawyer in the chief counsel's office would be reluctant to approve an injunction if they had replied to NECC's response to the warning letter. It seems like FDA's staff were considering—it seems like if they were—the FDA staff were considering serious enforcement actions like enjoining the company, but a breakdown in process was preventing the agency from taking decisive action. Is that a correct statement?

Dr. HAMBURG. As I said before, we should have been more prompt, but it is the case that during that period, there was a series of court decisions that were altering the landscape with respect to the application of relevant legislation with respect to FDA authorities, and that was, unfortunately, slowing our response.

I hope that we will not be in that situation again going forward, that is why I am here really saying that we do need strengthening and clarification of our regulatory authorities. We do need new laws that will enable us to be able to provide the clear, consistent, and uniform regulatory oversight and action with these compounding pharmacies that are making, as you point out, the higher risk sterile products.

Mr. HARPER. So in that situation, no matter the risk, FDA was not willing to do anything?

Dr. HAMBURG. You know, again I am a little bit uncertain about how much detail to speak to because of the ongoing criminal investigation.

Mr. HARPER. OK. The ongoing criminal investigation, which you have nothing in writing advising you of constraints for that, correct? You have said that there is nothing in writing. Do you have anybody here from the U.S. Attorney's Office that is here with you today to advise you on which questions to answer or not answer?

Dr. HAMBURG. No, I don't.

Mr. HARPER. Has there been any communication from the U.S. Department of Justice to this committee advising you what you should or shouldn't respond to?

Dr. HAMBURG. There has not been formal communication to this committee, no.

Mr. HARPER. I yield back.

Mr. MURPHY. Thank you. The gentleman's time is expired.

We will go through a quick second round of questions here, so let me begin here.

Commissioner Hamburg, obviously one of our key concerns here is that the FDA's process failed. For a year, inspections were suspended. I am not sure we still have a clear answer yet of when you became aware of that. And we also recognize this has gone on for 10 years. There is nothing political about this. This took place under different commissioners, different Administrations.

What I believe a number of us are concerned about is that while you were here asking for some new laws and new authority, I, for one, am not yet convinced that the FDA has taken steps to clean up its own house here. Inspectors wanted to go back and re-inspect. They were frustrated because of decisions by the Chief Counsel's Office to delay it.

Now, it would seem to me that a common sense next step would be for you to call together a post mortem after you became aware of all these problems. Get the people together responsible, and say who knew what and when and who made this decision and why. So I want to ask, have you gone back and had such meetings with your agencies, and have you done this post mortem and asked your staff to review the process that took place?

Dr. HAMBURG. We have looked very carefully back at some of the steps that were taken, decisions made, and as I said, I am troubled that we did delay because of internal discussions and conflict, and the changing legal landscape, and not being certain exactly what law we would be applying in different parts of the country, et cetera, so we have taken that deeper dive. We also have reorganized within FDA to try to strengthen our efforts in this area, and as you noted, have embarked on a much more aggressive effort to use our current and existing authorities.

Mr. MURPHY. I understand that, and you told us you embarked on a more aggressive effort. We have seen you doing more inspections now. You have acknowledged that, and you have made some recommendations to us about changes you want into law. What I am asking is have you had an internal formal investigation where you have addressed the issues that have taken place? For example, has anyone at the FDA at your request talked to the head of the Center for Drugs about the NECC or Ameridose cases in terms of what happened?

Dr. HAMBURG. We have internally had many ongoing discussions about not just the specifics of this case, but also the broader efforts with the compounding industry, and I think we all agree that the FDA could have done a stronger job, and that we are committed to doing so going forward, but to do the best job for the American people, we do feel that our regulations, the ambiguity of the statute, the——

Mr. MURPHY. I understand that, but I am trying to find out about the post mortem——

Dr. HAMBURG [continuing]. Different state laws, all compromise that.

Mr. MURPHY. I am trying to find out what the policy change within that—we will address the ambiguities and other things later, but did you talk to the head of the New England District Office since you became aware of the problems with NECC?

Dr. HAMBURG. I have talked—well, the head of the district office that you are probably referring to retired around that time, but we have had discussions and clearly we want to learn as much as we can about the inadequacies of past responses to the compounding pharmacy issues——

Mr. MURPHY. Well let me ask you this——

Dr. HAMBURG [continuing]. So we can do a better job going forward.

Mr. MURPHY. Listen, we are trying to help you. We really are. If you have done a post mortem, if you have done this analysis that for 10 years handcuffed the agency from moving forward because of internal decisions, there were multiple times that the FDA knew about problems taking place in states, but it appears that they didn't call Massachusetts or the states to say we got this complaint. You are the agency in charge. And I go back to when you say that you want them to report adverse events so you can mitigate as fast as possible. One of the ways to mitigate is to inform the states. You don't have to take other action, other than to pass that on. I am not sure yet I hear that there has been a change of policy. Has there been a change of policy with regard to notifying states of information you have received in complaints?

Dr. HAMBURG. We are actively engaged in that. Now, one thing we did was, in fact, to bring in all the 50 states soon after this event to start to talk about how to strengthen communication——

Mr. MURPHY. So there is no specific policy at this point to say when we get a complaint, that is to be passed on to the state of jurisdiction. Until such time we can clarify that you have authority, you know the states have authority. Do you have a policy in place that those complaints would be passed on to the states right away?

Dr. HAMBURG. There has been a reorganization and we have identified a new set of players to work on this, and we will be——

Mr. MURPHY. Who is that——

Dr. HAMBURG [continuing]. Beginning stronger follow-up with the states and we will be——

Mr. MURPHY. Is that an automatic process now?

Dr. HAMBURG. Pardon me?

Mr. MURPHY. Is it going to go through—because see, part of the problem here is it goes through—what we have heard from you is it goes through lots of chains of lawyers and discussions, and there is one year that no inspections were taking place, everything was on hold. There was a long period of time before a complaint was responded to, and what you are telling me is there is going to be more discussions. That does not satisfy this committee or the American public to know that you are going to have more discussions. They want to know about action. Do you have some automatic policies that you have authorized now when you receive com-

plaints from the states who have jurisdiction, you have said, that they automatically get that information?

Dr. HAMBURG. We have set up a structure to ensure that those kinds of communications occur. We also do try to respond and investigate——

Mr. MURPHY. Is it automatic?

Dr. HAMBURG [continuing]. Complaints that we get and adverse event reports that we get.

Mr. MURPHY. Would you give us any documents that describe that policy now, because I am not satisfied with saying you are going to try, you are going to review, you are going to discuss. I think this is what hamstrung the FDA up the last 10 years, and why in the words of one family who lost a loved one, they said they don't trust the FDA. If there is one federal agency among them all that we ought to have an inherent and implicit trust in, it should be the FDA, and I don't think that is there right now, so I would like you to share with us those policy documents so we could know that.

Thank you—and in a timely manner.

Ms. DeGette for 5 minutes.

Ms. DEGETTE. Thank you very much, Mr. Chairman.

The real issue here, Commissioner Hamburg, is what authority does the FDA have that they didn't exercise for whatever reason in the last 10 years, and what new authority does Congress want to give them? I never met a member of Congress on either side of the aisle who said, I think the agency should just go out and do whatever they want. We are always concerned that the agency acts within the authority that we give it. But if you already have the authority, we want you to exercise that. If you need a clarification, we want you to do that. I think that is pretty clear, correct?

Dr. HAMBURG. Correct.

Ms. DEGETTE. OK. So I want to talk to you specifically about the authority that you have, because Mr. Burgess, in his questioning, he accurately said that the FDA has authority over drug manufacturers, correct?

Dr. HAMBURG. Correct.

Ms. DEGETTE. But under that authority, that is not the authority that the FDA has over compounding pharmacies, is that correct?

Dr. HAMBURG. That is correct.

Ms. DEGETTE. And that is because the courts and others have determined that compounding drugs is not the same as manufacturing drugs, is that right?

Dr. HAMBURG. There are certain explicit exemptions for compounding pharmacies from the authorities we have over conventional drug——

Ms. DEGETTE. Right, and that is in Section 503A of the 1997 Food and Drug Modernization Act, right?

Dr. HAMBURG. That is right.

Ms. DEGETTE. So in 1997 when Congress enacted that law, we specifically set forth—we thought we specifically set forth what authority the FDA had over compounding pharmacies, correct?

Dr. HAMBURG. Correct.

Ms. DEGETTE. And what has happened since 1997, number one, the nature of the industry has changed. It is not just a mom and pop pharmacy down on the corner, right?

Dr. HAMBURG. Correct.

Ms. DEGETTE. And the other thing that has happened is that around the country, some of the compounding pharmacies have been aggressively challenging the FDA's authority even under Section 503A, right?

Dr. HAMBURG. That is very true.

Ms. DEGETTE. And that is what we talked about before with the confusing court cases, right? So now what happens is—and I want to say, I share everybody else's deep concern that the agency really fumbled around for about 10 years. OK, so now you come in and you say this is appalling. These people shouldn't be at risk, this poster over here with the black stuff floating, that is unacceptable. It is unacceptable. You agree with that, right?

Dr. HAMBURG. I absolutely agree with that.

Ms. DEGETTE. So now you are trying to take the authority we gave you under 503A and to inspect at-risk pharmacies, people that you think might have a trouble, right?

Dr. HAMBURG. Correct.

Ms. DEGETTE. And what you are saying to us is that these pharmacies are pushing back and they are saying that Congress did not give you the authority to conduct these investigations, is that right?

Dr. HAMBURG. Yes, and it is broader than that in terms of we don't have the authorities to have a regulatory regime that makes sense.

Ms. DEGETTE. OK. What is it specifically that you need, Commissioner Hamburg?

Dr. HAMBURG. We need these compounder of high risk products to register with us. We need——

Ms. DEGETTE. And how do you know what the high risk products are?

Dr. HAMBURG. Well, in order—we also need the authority—the high-risk products we define as—the highest risk, I think, are the sterile products. We all agree on that.

Ms. DEGETTE. OK.

Dr. HAMBURG. We need inspectional authority and full access to records in order to determine if a compounding pharmacy, in fact, is making products of concern, and how they are distributing, et cetera. Clearly, there should be a uniform set of standards for safety practices and quality manufacturing.

Ms. DEGETTE. OK. Do you know that you don't have those inspectional abilities now?

Dr. HAMBURG. Pharmacies are exempt in terms of full inspection requirements and access to records under section 704.

Ms. DEGETTE. OK, so the answer is yes, you know you don't have that authority, right? And what other authority do you need?

Dr. HAMBURG. We need—I mean, I sound a little bit like a broken record, but we need the authority for high risk manufacturers to register with——

Ms. DEGETTE. And then once they register, what will that do?

Dr. HAMBURG. Then we will know who they are and what they are making, how they are distributing, if they are selling to wholesalers, then they are behaving like a manufacturer, so——

Ms. DEGETTE. And then do you—once they register then, do you think if you get a complaint about them you have the authority to investigate them, or is that the second thing you were just talking about?

Dr. HAMBURG. We need the inspectional authority. We need the ability to have these clear standards that they will adhere to for safety and that we can inspect against and enforce against, and the adverse event reporting is very critical as well.

Ms. DEGETTE. And do you think that if we do some of this very targeted legislative language, that will help with what the chairman was talking to you about, about the tensions between the regulators and the lawyers and the agency, which is really of a concern to all of us?

Dr. HAMBURG. I think it absolutely will. You know, I think we allowed ourselves to be far too cautious because of fears of litigation that might actually further undermine our ability to apply authorities and take enforcement actions, and that should not happen. Public health should not be impeded by those kinds of legal regulatory ambiguities.

Ms. DEGETTE. Thank you very much. Thank you, Mr. Chairman.

Mr. MURPHY. Thank you. Now recognize again Mr. Griffith for 5 minutes.

Mr. GRIFFITH. And in fact, you have authority over manufacturers, isn't that true? Yes or no?

Dr. HAMBURG. Yes.

Mr. GRIFFITH. And with complaints from the State of Ohio indicating that they were—the manufacturing process going on—back to Ameridose, which is the sister of NECC, and the Cease and Desist from Colorado, Mr. Taylor, wouldn't have been that difficult to probably get—if they refused to let you in, wouldn't it have been that hard to get a warrant under your manufacturing authority, isn't that true, for both NECC and Ameridose?.

Mr. TAYLOR. I am not sure that—I mean, it takes more evidence than that, but let me just—to your point, communication with the states is one of the things that we recognize needs to be improved.

Mr. GRIFFITH. OK, but the bottom line is, you and I both know as practicing attorneys that it doesn't really take a very high standard to get a warrant to go and get information, particularly when the risk to the public is as great as it is when you are doing things with sterile injections. Isn't it true that it is a fairly low bar to get a warrant under these types of circumstances? Yes or no?

Mr. TAYLOR. No. It requires——

Mr. GRIFFITH. I respectfully disagree. I got to move on.

Mr. TAYLOR. All right.

Mr. GRIFFITH. I only get 5 minutes, so I would love to have that discussion with you sometime, but not today.

Mr. TAYLOR. That is fair.

Mr. GRIFFITH. I am concerned that you all were receiving—Dr. Hamburg, you all were receiving a lot of things—if you look at Tab 31 in the binder that is there on your table, and then you flip over to page 3, a summary would be that in July and August of 2008,

FDA came to Ameridose for inspection. The company performed—this is an informant's statement that was sent to you all that is in documents you provided us. In July and August of 2008, FDA came to Ameridose for an inspection. The company performed illegal and unethical actions. They directed the testing facilities to change reports based on the drug resorts. They forged documents. Now that was—the person was referring to July and August of 2008. This was received by you all, according to the information you sent us, in August of 2009. And after that complaint came in, FDA New England District Office Mr.—I don't want to—he may be a doctor but I can't tell here—Shamsi, after reviewing the complaint, sent an e-mail saying "we are waiting for assignment from the Center for Drugs to go out and we will follow up on this. Ameridose has been on our radar for quite some time."

Commissioner, nothing was done at that time to further investigate Ameridose, isn't that correct?

Dr. HAMBURG. You know, there was follow-up to many of the concerns that were raised.

Mr. GRIFFITH. OK. Can you provide that to us, because in the information we already have, there doesn't appear to be any follow up on that. Can you provide that to us, because apparently it was neglected—somebody neglected to give that to us before this hearing.

Dr. HAMBURG. I want to be clear——

Mr. GRIFFITH. Yes, ma'am.

Dr. HAMBURG [continuing]. That I do not feel that we responded adequately but that——

Mr. GRIFFITH. I am asking you to respond adequately to this committee and the documents that we have in the binder here don't show that you responded at all after that complaint came in in 2009, even though your New England District Office was asking for clearance to respond. "We are waiting for an assignment from the Center for Drugs to go out and we will follow up on this. Ameridose has been on our radar for quite some time." And you didn't follow through, unless you have got documents we don't have that you failed to give to us.

Dr. HAMBURG. What I am saying is that we get a lot of complaints and——

Mr. GRIFFITH. So more authority really wouldn't do you any good?

Dr. HAMBURG. I can't speak to the specifics there, but there is just no doubt that, I don't think that we responded with the vigor that we should have. I do think that we were——

Mr. GRIFFITH. So now you are saying that you didn't follow up on that?

Dr. HAMBURG. No, I am saying that I can't speak to the specifics of——

Mr. GRIFFITH. All right.

Dr. HAMBURG [continuing]. All of the 30,000 pages of documents.

Mr. GRIFFITH. All right. You also received information, and that would be Tab 32, an internal source at Ameridose raised in July and August of 2010, and the source was identified as a pharmacist in the notes that you have given to us, and according to a memorandum of conversation between the pharmacist and a compliance

officer, the pharmacist said that "Ameridose personnel from their sales force were assisting in labeling"—and this is sales force—"assisting in labeling operations in the clean room, and that one of the three clean rooms had a result for positive mold growth." Now, the sales force is not supposed to be involved in that, according to other documents. That is correct, isn't it? They are not supposed to be cleaning up and labeling things, they are supposed to be selling.

Dr. HAMBURG. Right.

Mr. GRIFFITH. And yet, there is a note here that there was a positive result for mold growth. That individual was told that the FDA takes this seriously. There is an e-mail in that Tab 32, that "this is taken seriously. Mold growth can affect sterility of drugs." Now remember, this is the sister to NECC. It is usually taken seriously by the FDA, but the FDA didn't follow up, so it wasn't taken seriously in this case, was it, ma'am?

Dr. HAMBURG. I cannot speak to the specifics of that instance, but those kinds of concerns are concerns that would worry me then, and certainly worry me now. There are, unfortunately, too many ongoing problems with compounding pharmacies, and I really do feel strongly that if we are going to be——

Mr. GRIFFITH. But Ameridose was——

Mr. MURPHY. Gentleman's time is expired.

Mr. GRIFFITH [continuing]. Also a manufacturer, was it not?

Mr. MURPHY. Gentleman's time is expired.

Mr. GRIFFITH. I apologize, Mr. Chairman. I yield back.

Mr. MURPHY. Gentleman from Michigan, Mr. Dingell, is recognized for 5 minutes.

Mr. DINGELL. Thank you, Mr. Chairman.

Dr. Hamburg, we have here before us a most interesting circumstance. You have got a recalcitrant industry, trade association that is circularizing folks as to how they can frustrate Food and Drug, and its examination of their businesses and their protection of consumers. They are instructed as to limitations on Food and Drug's authorities. They are also—we also find that they are diligently at work to get the powers of Food and Drug curtailed. And to see to it that legislation as was done here specifically exempts them from three critical provisions: premarket approval of new drugs, requirement that drugs be made in compliance with good manufacturing practices standards, and the requirement that the drug bear adequate directions for use, i.e., your labeling requirements.

Have those situations caused you difficulty at Food and Drug as you go about your business trying to regulate these good-hearted folk?

Dr. HAMBURG. We do not have the same kinds of problems with conventional manufacturers——

Mr. DINGELL. I understand that, but——

Dr. HAMBURG [continuing]. As we have with compounding pharmacies.

Mr. DINGELL. But you have huge problems with the compounders, do you not?

Dr. HAMBURG. We do.

Mr. DINGELL. Unsafe clean rooms, pharmaceuticals that are compounded with all kinds of things, including filth and other things in them, dust spots and things of that sort, am I right?

Dr. HAMBURG. That is correct.

Mr. DINGELL. OK. So you don't have authority to require them to register so you know who is in the business, right?

Dr. HAMBURG. Correct.

Mr. DINGELL. States have a somewhat varied record on these matters. Michigan has five people who are looking into this, is that right? And Michigan's folk cannot go across the borders of the State of Michigan to look see what those good-hearted folks in Massachusetts are doing to kill off Michigan's citizens by unsafe pharmaceuticals, is that right?

Dr. HAMBURG. You know, I am not familiar with the specifics of state laws, but it creates a real—we have heard from the states that they don't feel that they can provide adequate regulatory oversight of what is happening in pharmacies in other states——

Mr. DINGELL. Now, you have no authority to get in books and records and to inspect compounders, is that right?

Dr. HAMBURG. We are limited in our access to records.

Mr. DINGELL. All right. And you have no authority to inspect a business according to what they circularize their memberships from the trade association, is that right?

Dr. HAMBURG. That is right.

Mr. DINGELL. Now, you had no authority to require information on adverse events, right?

Dr. HAMBURG. Correct.

Mr. DINGELL. So on that wonderful event that occurred up in Massachusetts where they shipped all this bad stuff around to Michigan and other places, they had no requirement and no responsibility to circularize—rather, to inform you of the events that occurred, is that right?

Dr. HAMBURG. That is right.

Mr. DINGELL. And you had no authority to extract it from them, is that right?

Dr. HAMBURG. No authority to inspect—to fully inspect?

Mr. DINGELL. You had no authority to compel them to present that information, is that right?

Dr. HAMBURG. That is correct.

Mr. DINGELL. OK. And you have no requirements for good—you have no ability to impose good manufacturing practices on them?

Dr. HAMBURG. Pharmacies that are exempt under existing legislation, we don't have that authority.

Mr. DINGELL. And good manufacturing practices are absolutely critical to seeing to it that the pharmaceuticals are safe, is that not so?

Dr. HAMBURG. Good manufacturing practices are essential.

Mr. DINGELL. All right. And you—do you have the resources, the monies that you need to properly police the behavior of these organizations?

Dr. HAMBURG. We do not have the resources that would be necessary to put in place the kind of strong regulatory oversight we need.

Mr. DINGELL. At what point does it cease to be compounding and become manufacturing?

Dr. HAMBURG. Well——

Mr. DINGELL. There are good-hearted folks up in Massachusetts who were churning out stuff by the thousands, and you couldn't find out who they were, you couldn't find out what they were doing, you couldn't impose good manufacturing practices on them, but at what point could you have—could they have been charged with being manufacturers? They are shipping all over the country.

Dr. HAMBURG. Yes, it is an issue where people think it is black and white. Either you are a compounding pharmacy or a manufacturer, but that has been at the root of many of these problems in terms of the conflicting court decisions, and it is not written in the statute.

Mr. DINGELL. Do you have——

Dr. HAMBURG. The statute is ambiguous.

Mr. DINGELL. Do you have the personnel to inspect these people?

Dr. HAMBURG. We don't have the personnel to inspect all the——

Mr. DINGELL. OK. Now Doctor, do you have the authority to ban bad actors?

Dr. HAMBURG. Not directly.

Mr. DINGELL. These——

Dr. HAMBURG. The compounding pharmacies are licensed by the states.

Mr. DINGELL. You have got these people in Massachusetts that are creating thousands of prescriptions that are being distributed all over the country, clearly to me, that are bad actors. You have virtually no authority of them. What can you do about them?

Dr. HAMBURG. Well, I think that if we want a system that is really preventive and protects against problems and ensures safety, we do need new legislation. I think that——

Mr. DINGELL. What authority——

Mr. MURPHY. Gentleman's time is expired.

Mr. DINGELL. What authority do you have to supervise to see to it that stuff moving across the state lines that is supposed to be supervised by the states, which can't do it, is, in fact, not something that is going to create safety problems for people? Now would you just submit the answer to that for the record?

Dr. HAMBURG. OK.

Mr. DINGELL. Mr. Chairman, you have graciously given me a minute more than I am entitled to.

Mr. MURPHY. I thank the gentleman. Now I recognize the gentleman from Texas, Mr. Olson, for 5 minutes.

Mr. OLSON. I thank the chair and I yield to him as much time as he may consume.

Mr. MURPHY. Thank you. I appreciate that.

Ms. Hamburg, you have said repeatedly in one version or another you feel you don't have the authority to have strong oversight. My concern remains that where you do have authority, you haven't had that kind of oversight that you can exercise, except for the recent flurry of well-publicized inspections.

Let me run through some specifics here to again illustrate my concerns of the agency for 10 years, and hopefully your comments

of what you have done to rectify that, within the authority you have now.

The FDA inspected NECC in 2004, primarily in response to complaints related to the company soliciting a product being used in cataract surgery. You may recall that, if you reviewed that. The violations letter the FDA observed during that inspection were finally addressed over 2 years later in a warning letter issued in December of 2006. That warning letter noted the concerns about NECC and mentioned the fact that NECC was reportedly informing patient's physician's offices that patient-specific prescriptions were not required. Do you recall that from history? OK. It wasn't under your administration, but I just wanted to make sure you knew that.

NECC responded immediately in January 2007, noting that it had been over 2 years since the FDA had been at their facility and rejecting a number of FDA's charges. Is that correct?

Dr. HAMBURG. Yes.

Mr. MURPHY. Now, at Tab 16 in your binder, if you look at it there, Steven Silverman, who was then the director of the Division of New Drugs and Labeling Compliance at FDA's Center for Drugs thought that "NECC's response was unacceptable." Do you agree that staff appeared frustrated with the fact that it took chief counsel's office 2 years to issue the warning letter?

Dr. HAMBURG. Yes.

Mr. MURPHY. And this frustration appears to have been shared by Deborah Autor, the head of the compliance at FDA's Center for Drugs at the time. In an e-mail to Mr. Silverman, which is located at Tab 17, Ms. Autor stated that they have "completely lost sight of the point that the warning letters are intended to quickly get word to violators that they need to come into compliance. Instead, the lawyers are concerned about perfecting documents that quickly become irrelevant." Now, do you agree with this observation that concerns about perfecting documents have resulted in delay when issuing warning letters?

Dr. HAMBURG. I am concerned when there are those kinds of delays.

Mr. MURPHY. The key is does that mindset still exist today?

Dr. HAMBURG. I think that the mindset is very different. I think we are determined to use the authorities that we have to the greatest degree that we possibly can, even in the face of challenges to our authority, and in the face of potential inability to actually be successful in some of our enforcement actions. We are doing inspections now. We are finding things that are of serious concern. We intend to pursue those concerns, and already there have been recalls and other actions taken. But we intend to use the authority we have to the greatest degree possible. But I am deeply concerned that we don't have the authorities we need to have the kind of system in place that will provide better protection and that will reduce the kinds of problems that we are seeing that could put people at risk in the future.

Mr. MURPHY. Did the FDA have the authority to suspend inspections in 2011 and 2012 for NECC?

Dr. HAMBURG. I think what happened there was what happened in other instances as well where unfortunately because of a lack of

clarity about what should the regulatory and enforcement framework be that we slowed down. We weren't as aggressive as we could have been, and I regret that.

Mr. MURPHY. What other instances——

Dr. HAMBURG. But I don't think that we have a system now in terms of the authorities that are available to us that is sufficient for these highest risk manufacturers making the sterile products.

Mr. MURPHY. So have you identified who made this decision that the inspections wouldn't take place against NECC in 2011, 2012 in your post mortem? Have you determined who that was?

Dr. HAMBURG. There was an ongoing debate that was reflecting the fact that decisions—a series of legal decisions had come down. There was an issue about whether to go to the Supreme Court to try to resolve the circuit court split, and then we were sort of left with the map and trying to determine what was the best way to develop the enforcement——

Mr. MURPHY. So given that, have you gone back in to see if there are any stalls or other problems like that with other companies under—who are compounding pharmacies? I know you just did a bunch of inspections. Have you gone back to see if those conditions exist for any other pharmacies?

Dr. HAMBURG. I am sorry, in terms of——

Mr. MURPHY. Well, did any other——

Dr. HAMBURG. During that period, we were not aggressively pursuing compounding pharmacies in a proactive way. We were responding when complaints came to us. We were, in fact, engaged in some litigation around compounding pharmacies, and sadly, one that we thought was one that would be very successful and we lost, all of that was contributing to the sense that the uncertainty and ambiguity in the law and the patchwork of applications of this law was making it harder for us to do our job.

Mr. MURPHY. I appreciate that, and I know that the concern still from the American public is these discussions are taking place, lawyers, et cetera, but still, it wasn't addressing your primary mission as taking care of some of the public's health first. But we will continue to talk about that.

Mr. Waxman is recognized for 5 minutes.

Mr. WAXMAN. I thank you, Mr. Chairman. I haven't been here throughout the whole hearing, but I find it hard to understand why anyone would argue with you that you had enough authority under the law, when it is clear that two different circuit courts have said different things about a law, and limited the amount of actions you can take. For example, under existing law, under the underlying law itself, you can't have sample collections, you can't—just go through some of the things you cannot do.

Dr. HAMBURG. Under 503A?

Mr. WAXMAN. Yes.

Dr. HAMBURG. Well, there is, of course, the broader issue——

Mr. WAXMAN. Let me—look. This is not where I wanted to go with my questions, but there are so many things you cannot do, including some things my staff pointed out to me, and I wrote it down and I can't read my writing. But——

Dr. HAMBURG. Well, I am happy to discuss——

Mr. WAXMAN [continuing]. It is hard for any reasonable person to not conclude you need a stronger, clearer law to give you authority.

People want to go over the history, and so I want to ask you about the history of the Obama Administration. I mean, this started much before, but in 2009, the Obama Administration entered office. For 7 years, the Bush Administration had been stymied by a series of conflicting court decisions and inherently weak laws. So leaders at FDA met in the spring of 2009, and according to the notes of the meeting, the participants acknowledged the risks of compounding and sent forth a new path for a national policy. Ultimately, they decided to implement Section 503A nationwide, except in the Ninth Circuit. And there they would implement a compliance policy guidance based on Section 503A. Most of these decisions were made before you were confirmed, isn't that correct?

Dr. HAMBURG. That is correct.

Mr. WAXMAN. But can you elaborate on why, in your understanding, the agency made those decisions?

Dr. HAMBURG. Well, I think that we were faced with a situation where we felt we did need to do more, and there was a lot of eagerness as reflected in the documents to do more, and we needed to determine the legal framework that we would be applying. We needed to——

Mr. WAXMAN. You were looking for the most legally defensible way to develop a coherent and rational policy.

Dr. HAMBURG. Well, that is absolutely right, and I——

Mr. WAXMAN. And so as you looked at different alternatives, you said well, we can't do this and we can't do that. Is that right?

Dr. HAMBURG. That is absolutely right.

Mr. WAXMAN. Can you help us understand what FDA's concerns were about going forward with inspections and potential enforcement actions before releasing a new compliance policy guidance that would give a coherent national policy to address conflicting court cases? You were asked earlier why the agency couldn't walk and chew gum at the same time; that is, conduct the inspections while developing the CPG. I assume the agency had compelling concerns about the problems it would encounter if it had conducted those inspections. Can you describe them for us? I would like to address this question Mr. Taylor, because he is the enforcement expert.

Mr. TAYLOR. I am sorry, I was——

Mr. WAXMAN. OK, put your mike on, first of all. And what I want to know is why couldn't the agency go forward with the inspections at the same time you are doing a CPG?

Mr. TAYLOR. Well, the—and I wasn't there, but the people were worried that if they moved ahead with actions with the circuit courts split and without clear guidance, that it would lead to losses in court, some losses that would possibly undercut the authority that the agency had further. So there was a fear that it could actually make this unsettled legal landscape even worse, and it appears from the documents that that accounts for some of the conservative—which we regret, which is why we are being more aggressive now.

Mr. WAXMAN. Right, why you are here and why you have to answer questions. I know one thing, if you had acted, you know what would have happened? The compounding industry would have clear ordered their—they would have alerted all their members. They would have aggressively pursued back in the public and on the Hill, to push back on you. Maybe you would have gone to court, maybe they would have sued you to go to court to challenge what you were doing. FDA probably would have faced pressure from members of this body to pull back. In hindsight, it is easy to blame the FDA, but in the real world, prior to that outbreak, it would have been very hard to do this.

One internal document said the agency intended to release the guidance by December, 2011. The subsequent internal document indicated the agency was trying to get the document cleared by September, 2012. October came and went. Dozens of people died in the meningitis outbreak, and still FDA showed no guidance. So my question is what happened here? Why did it take the agency this long to get the guidance out? Had you gotten the guidance out, do you think you could have prevented the meningitis outbreak? Can you describe what the guidance would have accomplished, and can you describe what the guidance would not have been able to do, and would have the guidance eliminated the need for new legislative authority that you now seek?

Dr. HAMBURG. It took too long to get the guidance out, but it is important to understand what the guidance actually represents. It is just that. It is guidance to industry about how we would be approaching regulation in this area. But the guidance is only as strong as the underlying statute. It cannot substitute for a strong, clear law. You cannot fill gaps in the law with guidance, and so it was an imperfect second to what we really need and what we are hoping to work with all of you to do, which is to get the kind of strong, clear law that is necessary to put in place a program that is comprehensive in terms of the kinds of authorities we don't have now, that focuses on the highest risk producers of the sterile products, and that will enable us to really work with industry in a preventive way, rather than being forced into a situation where we are more reactive than we should be.

Mr. WAXMAN. Yes, I thank you.

Let's work on that law, Mr. Chairman.

Mr. MURPHY. Thank you, Mr. Chairman.

Mr. Johnson, 5 minutes.

Mr. JOHNSON. Thank you, Mr. Chairman.

Commissioner Hamburg, despite your assertions at the last hearing that FDA really doesn't know how many compounding operations were out there because they didn't have access or didn't have to register with the agency, FDA has recently embarked on a sweeping risk-based inspection campaign, targeting approximately 50 facilities, primarily of large scale compounding operations. Is that right?

Dr. HAMBURG. That is correct, but it is not because they have——

Mr. JOHNSON. OK, good. Commissioner Hamburg, then in your opinion, how many of these companies have been operating in the shadows?

Dr. HAMBURG. We targeted these inspections—about 31 of those inspections were surveillance. Others—the rest of them—were for cause when problems were brought to our attention, but we targeted them based on information that had come to us about concerns that they were making sterile products; but that is not an adequate approach when it comes to really being able to have a regulatory system that enables us on a routine basis to go in and do inspections, and as I said, to work in a way with the companies so that problems can be prevented.

Mr. JOHNSON. So how did you determine which facilities to inspect?

Dr. HAMBURG. It was a risk-based determination, using information from different sources——

Mr. JOHNSON. So it is safe to say that——

Dr. HAMBURG [continuing]. From what states were telling us——

Mr. JOHNSON [continuing]. Many of these companies had long been on the agency's radar, correct?

Dr. HAMBURG. Some of them had been. Some of it was based on what states had told us. Some was public information from the media.

Mr. JOHNSON. Public information from the media?

Dr. HAMBURG. But we would like——

Mr. JOHNSON. Had you received event reports—I think that is what we call it—earlier? Had you received reports from——

Dr. HAMBURG. I don't believe we had for all of the facilities that we inspected. I would have to go back and ask——

Mr. JOHNSON. Well what I am trying to figure out is you didn't choose to inspect NECC and you didn't choose to inspect Ameridose, but you chose to inspect all of these others, and you don't even know whether or not there were event reports associated with them, so what I would like—if you would take this for the record, to provide this committee with all the complaints that the FDA has received associated with their products and practices, because I think the committee could be enlightened by what your standard or what your water level is to determine who you are going to inspect and who you are not. I would like to see that, and I think many of my colleagues here on the committee would too. That would be edifying to us, because there is a real—because I am sort of alarmed by what you just said that many of them did not have event reports.

Dr. HAMBURG. It is not required for these facilities to provide us——

Mr. JOHNSON. I didn't say it was——

Dr. HAMBURG [continuing]. Provide us with——

Mr. JOHNSON. I didn't say it was required. That is a judgment call, apparently, on who you inspect and who you don't, and you made the decision not to inspect NECC or Ameridose, but you chose then since the outbreak to inspect these other 50. I want to see what the criteria is. What causes you enough alarm to want to go inspect, and if event reports, let's say public health is in danger and that lives are in danger, if that is not enough, I would like to be able to understand that.

Dr. HAMBURG. Well, I—what I am saying to you is that we need to have a system that actually requires these compounding pharmacies to register with us so that we will know——

Mr. JOHNSON. We are not talking about——

Dr. HAMBURG [continuing]. Who they are——

Mr. JOHNSON [continuing]. The ones that didn't register. We are talking about the 50 that you chose to inspect. What was the criteria——

Dr. HAMBURG. We chose to do that in lieu of having information that we think should be part of a strong and meaningful regulatory scheme going forward——

Mr. JOHNSON. But what was the criteria used, and how does that balance against the criteria of the multiple event reports that you received on Ameridose? So I—can you take that for the record and——

Dr. HAMBURG. We can certainly take that for the record and, I think this goes to the heart of some of our concerns about what we need to do to have the kind of safety net in terms of——

Mr. JOHNSON. The heart of my concern is the judgment. The heart of my concern is the judgment used by the FDA to decide who to inspect and who not to inspect, and based upon your testimony here now, I have even further questions about that because you just said that many of the new 50 that you are inspecting did not have event reports associated with them. So I am really confused how, with as much advanced notice and concern that you had about Ameridose, that something didn't trigger with your organization and you said the buck stops with you, how that did not trigger something at the FDA that that company needed to be inspected?

So to be clear, I need you to provide the committee, if you would, please, all of the complaints that the FDA had that led you to—with their products and practices that led to the selection of those 50 that you chose to inspect.

And with that, I yield back, Mr. Chairman.

Mr. MURPHY. Gentleman yields back. Now recognize the gentlelady from North Carolina, Ms. Ellmers, for 5 minutes.

Mrs. ELLMERS. Thank you, Mr. Chairman.

II would like to follow my colleague from Ohio. Of the 50 that were inspected, were they all registered with you, with the FDA?

Dr. HAMBURG. No, they were not. That is what I am saying is we need——

Mrs. ELLMERS. OK, you just went in and inspected and chose to inspect those. So I don't understand how, then, you keep reflecting back on the fact that you did not have the authority to inspect the numerous complaints that we have received here about Ameridose and NECC. How then——

Dr. HAMBURG. I didn't say we didn't have the authority, and I said I regretted that we didn't, in some of the instances, go back in more quickly.

Mrs. ELLMERS. But you didn't have the authority—and there again, I am just jotting down notes here. So you felt you didn't have the ability or authority to intervene with Ameridose? OK. Let's get back to the common sense of this. There have been numerous complaints which over a 10-year period had been submitted. They were submitted to you, the FDA, things that were

taking place in these facilities. Somehow, there should be that communication with the state. Of the complaints that were submitted, which ones were reported to the state, and when?

Dr. HAMBURG. I indicated that we would try to go back and look at that, but I——

Mrs. ELLMERS. OK. Were any submitted to the state? Were any complaints then passed on to the state?

Dr. HAMBURG. In certain instances, we actually went in with the state to do inspections.

Mrs. ELLMERS. In certain instances you did go—OK. I do want that for the record. I would like for you to submit the complaints that were passed on to the state and the number of inspections that took place with the state into these facilities, especially the Ameridose and the NECC.

Now having said that, is there a law in place now that prevents you from sharing information?

Dr. HAMBURG. No.

Mrs. ELLMERS. Legislation, law, regulation, guideline that prevents you from sharing information——

Dr. HAMBURG. With the states?

Mrs. ELLMERS [continuing]. With the states?

Dr. HAMBURG. No, and I think that that is an area where we are trying to do a much stronger job.

Mrs. ELLMERS. So there wasn't anything preventing you, but you want to do a better job. How do you do a better job if there wasn't anything preventing you?

Dr. HAMBURG. I am just saying that as I look back over some of the——

Mrs. ELLMERS. This was an area of failure.

Dr. HAMBURG [continuing]. Issues, that I think that we could definitely benefit, all of us, by working more closely, having more systematized mechanisms——

Mrs. ELLMERS. Because you have noted over and over again the state has the authority, the licensure ability, the regulation for the state, and yet, there seems to be this barrier there for sharing information that had been given to you, privy to you.

Now, let's back up to some of the complaints here. I just want to point out a couple, and this had to do with Ameridose. In one of the instances here, it says the "FDA received another call from Ameridose, informant alleging that not only was the Ameridose sales team assisting in labeling in the clean room, but that one of the three clean rooms had a positive result of mold growth." Let me further that. That was August, 2010. Another from August, 2010, "Informant called again a few days later, stating that the mold was found in the hood in which operations took place." Dr. Hamburg, what is mold?

Dr. HAMBURG. Mold is an organism that can cause diseases——

Mrs. ELLMERS. And what kind of disease? What is mold specifically?

Dr. HAMBURG. Well, my microbiology days are long behind me, but it is a micro-organism——

Mrs. ELLMERS. It is a fungus.

Dr. HAMBURG. Well, OK.

Mrs. ELLMERS. It is a fungus. So you will acknowledge that it is a fungus? August, 2011, an Ameridose informant notifies FDA "when packaging was dropped on the floor, employees are told to pick it up and ship." He further stated that "the bubble wrap is stored directly on the floor and that this room is dirty and never cleaned." I can go on and on. There is also an incident after the event, after 53 Americans died as a result of the failures of these facilities, that there were dead birds found in that facility. Dr. Hamburg, what kinds of diseases can result as of human contact with bird feces or droppings?

Dr. HAMBURG. Clearly, there are serious medical conditions——

Mrs. ELLMERS. Fungal diseases.

Dr. HAMBURG [continuing]. And clearly, the kinds of environmental exposures you are describing are not acceptable to sterile practice.

Mrs. ELLMERS. Absolutely not, completely and totally. And that is where I get back to the common sense factor here. When these things have been reported to you, how could it possibly be that they were not relayed on to the states?

And with that, I use up the remainder of my time. Thank you, Mr. Chairman.

Mr. MURPHY. Thank you. Now recognize Dr. Burgess of Texas for 5 minutes.

Mr. BURGESS. Thank you, Mr. Chairman, and Director Hamburg, thank you for being with us through this long session.

When Ms. Ellmers was just talking about picking up of the product that had fallen on the floor and then was retrieved and still shipped out, it made me remember in this very subcommittee, probably 4 years ago, Mr. Parnell of the Peanut Corporation of America undertook the same sort of practice in his peanut factory, and the consequence was a significant salmonella outbreak that sickened and I think killed some patients. Mr. Parnell is now in jail. So I mean, this is—he had been indicted. All right, I stand corrected. He should go to jail. But I mean, those are peanuts to make peanut butter. This is a sterile injectable to go into the subdural space or the epidural space of a patient. And so it is equally, if not much more, serious what Ms. Ellmers was just bringing up.

I do want to say for the record, early on in this process and in September of 2012, I want to acknowledge the help that the CDC provided our office when it was just almost impossible to get any phone calls returned or any information. The doctors at the CDC actually walked me through what they thought was going on, and I have to say, they did an excellent job of rounding up patients and getting people in for testing. I had—it had been a long time since I had been in microbiology, too. I don't think I even encountered—while I was in microbiology, but they did a very good tutorial for me on just what that organism was, how dangerous it was, even though it was one that wasn't normally thought of as a pathogen.

I know we have been through a lot of this stuff over and over and over again, and this stuff with Ameridose just—we keep coming back to it and I recognize a lot of it happened before you became administrator, and so I will stipulate that. But in July of 2011, you were the administrator, and in an exchange of e-mails that is in your binder there, Tab 37, there was a lot of discussion

about, once again, there are problems that have come up at Ameridose. I think it is Paige Taylor, a lawyer who sort of re-documented all of the problems that were there, and she sent that in an e-mail to the FDA's chief litigator. And the FDA's chief litigator, when she asked should we not re-inspect, I mean, I think he said well, it is CDER's call, but if the problems are serious safety issues, why would we only issue a warning letter? Why not seize? So that is a valid question. I mean, at this point, in July of 2011, the evidence is finding that there is a problem. Ameridose has come across the screen so many times. Your own chief litigator said why are we doing another warning letter? Why don't we just go in there and shut them down? So why not?

Dr. HAMBURG. Well I think that there was, again, internal discussion about how we should proceed, and I wish that we had been more aggressive, but I am saying we are going to be more aggressive now. And you mentioned the Peanut Corporation of America example. That is an example where actually in working with Congress, we were able to get the additional legislation, the Food Safety Modernization Act, that gave us new tools to work with companies to prevent problems and to really address some of those kinds of concerns, and I think that is not——

Mr. BURGESS. Well, let's not wax too eloquent, because we still have salmonella outbreaks and we all recognize that, but we all recognize that there were problems that needed to be addressed.

Your chief litigator went on to say my concern is that if we just issue a warning letter under one legal theory, and either do nothing until we issue the guidance, which apparently will take forever, or as noted below, would put another nail in our consistent policy coffin. I mean, those words were kind of prophetic, weren't they?

I will accept the fact that you acknowledge that the agency was far too cautious and that you are accepting some responsibility for that—being that risk averse. But I just got to tell you, I disagree with Mr. Waxman on the issue of the circuit court split. I mean, yes, there is a reason to protect their traditional compounding pharmacists. I used them when I was in medical practice. They fill a niche that needs to be filled, but the FDA has known for years that New England Compounding Corporation and Ameridose were not the mom and pop compounding. They were not traditional compounders in any conceivable definition. And I guess the concern as we wrap up this hearing, it does seem that at the agency the priority was on perfecting the policy or perfecting the policy guidelines, and not on protecting the patient. And if we learned nothing else from this today, it is that the mission of the Food and Drug Administration should be, first and foremost, on patient safety. The policy will always work itself out if we keep that number one objective in mind.

Mr. Chairman, you have been very generous with the time. I don't know if the commissioner wishes to respond, but I will be happy to yield back my time.

Mr. MURPHY. I thank the gentleman and on his behalf, Commissioner, do you want to answer that question?

Dr. HAMBURG. I just wanted to underscore what Dr. Burgess said, that I agree that patients and public health have to be our first priority, and I want to assure you that we are going to be as

aggressive as we can be with our current authorities, and that if you give us additional authorities that we feel we need to do the best job possible for the American people, we will use them.

Mr. BURGESS. I just have to say, it is going to take—that takes a lot of time, and you know that. You know what the political environment is here in Congress. Why not just use the authority that you have? Don't ask us for another tool when you have existing tools. My old daddy used to say, it is a poor worker who blames his tools. Don't blame your tools. Do your work.

Dr. HAMBURG. I think we need new tools.

Mr. MURPHY. Well, to that, I want to thank you for coming today and sitting through two rounds of questions, and for the members' devotions to this hearing today.

The committee rules provide that members have 10 days to submit additional questions for the record to witnesses. Let me say something very important about that. It was brought to our attention earlier today, Mr. Dingell and other members had asked questions last November. This is an opportunity to prove that the culture delay within the FDA has changed, because even with this committee, it has not. So I ask you to get the answers to the committee questions from last November to us by the 19th of April, and the members, since they have 10 days to submit questions to you, that you get back to us within 30 days of that date. It is important, because otherwise it leaves us thinking that delays continue.

I also ask unanimous consent to put the following documents into the record: the document binder at the witness table, subject to appropriate redactions by staff; opening statements of members; and the reports issued by Majority and Minority staff for this hearing, including the report from Mr. Markey, the Minority staff report of April 15, and the Majority staff report of April 16.

[The information appears at the conclusion of the hearing.]

Mr. MURPHY. Again, I thank all members for coming here, and with that, this hearing is adjourned.

[Whereupon, at 1:00 p.m., the subcommittee was adjourned.]

[Material submitted for inclusion in the record follows:]

Edward J. Markey Opening Remarks
"A Continuing Investigation into the Fungal Meningitis Outbreak and Whether It Could Have Been Prevented."
Oversight and Investigation Subcommittee Hearing
Tuesday, April 16, 2013

Last fall an outbreak of fungal meningitis stunned the nation, and thus far claimed the lives of 53 and sickened 733 in 20 states.

At the center of this tragedy was New England Compounding Center located in my district in Framingham, Massachusetts.

Tragically, this wasn't the first time NECC has produced tainted drugs.

But as with many other compounding pharmacies, when FDA tried to crack down on the activities of this facility, FDA's authority was challenged.

The compounding pharmacy industry has argued that all pharmacy compounding regulation should be left to the states. This industry has also lobbied aggressively to prevent Congress from enacting legislation that would give FDA more authority.

Yesterday, I issued a report [HOLD UP REPORT] showing that most states have no idea how many pharmacies in their States are compounding drugs in the first place.

They have no idea how many pharmacies are compounding sterile drugs. They have no idea which pharmacies have had repeated safety violations. They have no idea which pharmacies are shipping large volumes of drugs across state lines.

And they do not even provide the small handful of inspectors they have with the training they need to effectively inspect the riskiest facilities.

Not even Massachusetts, which now has in place the most stringent compounding regulations for drugs made INSIDE the state, can effectively oversee drugs sent INTO the state.

This is why FDA must be given clear and strong authority to ensure the safety of these drugs. The States simply cannot do it alone.

FRED UPTON, MICHIGAN
CHAIRMAN

HENRY A. WAXMAN, CALIFORNIA
RANKING MEMBER

ONE HUNDRED THIRTEENTH CONGRESS

Congress of the United States
House of Representatives

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Minority (202) 225-3641

MEMORANDUM

April 15, 2013

To: **Democratic Members and Staff of the Subcommittee on Oversight and Investigations**

Fr: **Energy and Commerce Committee Democratic Staff**

Re: **Hearing Titled "A Continuing Investigation into the Fungal Meningitis Outbreak and Whether It Could Have Been Prevented"**

On Tuesday, April 16, 2013, at 10:00 a.m. in room 2123 of the Rayburn House Office Building, the Subcommittee on Oversight and Investigations will hold a hearing on the regulation of pharmacy compounding following the deadly meningitis outbreak that began in September 2012. The outbreak resulted from contaminated steroid injections produced by a compounding pharmacy known as the New England Compounding Center (NECC).

The first case of meningitis linked to the injections was reported to the Centers for Disease Control (CDC) by the Tennessee Department of Health on September 21, 2012; within a week, the first case and numerous other cases had been linked to injections from NECC. To date, there have been 733 confirmed cases and 53 deaths across 20 states.[1] The Food and Drug Administration (FDA), the Department of Justice (DOJ), the Massachusetts Attorney General, and states across the country are conducting criminal investigations into the circumstances surrounding the outbreak.[2] These investigations are ongoing.

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[1] Centers for Disease Control and Prevention, *Multistate Fungal Meningitis Outbreak investigation: Current Situation* (Apr. 13, 2012) (online at www.cdc.gov/HAI/outbreaks/currentsituation/).

[2] *See Feds Open Criminal Inquiry Into Firm Linked to Deadly Meningitis Outbreak*, CNN (Oct. 23, 2012); *Mass. AG Enters Probe of Meningitis Outbreak*, Boston Globe (Oct. 11, 2012); *U.S. States Raise Heat on Company Linked to Deadly Meningitis Outbreak*, Reuters (Oct. 13, 2012).

This hearing is the second on this subject in the Energy and Commerce Committee. In November 2012, the Committee held a hearing titled "The Fungal Meningitis Outbreak: Could It Have Been Prevented?"[3] In the months since the November 2012 hearing, FDA responded to a bipartisan Committee request and provided over 27,000 pages of documents regarding the agency's prior interactions with NECC and its related companies. The documents included a record of past engagement with the companies, e-mails and correspondence within the FDA discussing how to deal with NECC and an affiliated compounder, Ameridose, and internal documents from FDA discussing the current regulatory framework applicable to compounding pharmacies.

The hearing will address questions about whether FDA appropriately regulated NECC and whether FDA needs additional legislative authority to address the risk of pharmacy compounding effectively in order to prevent another public health crisis.

I. NOVEMBER 2012 SUBCOMMITTEE HEARING ON THE MENINGITIS OUTBREAK

The November 14, 2012, hearing examined past interactions between regulators, NECC, and affiliated companies in order to understand what actions state and federal authorities could have taken to prevent the outbreak. NECC, and its sister companies, Ameridose and Alaunus had been the subject of state and federal inspections, oversight, and enforcement on numerous occasions prior to the outbreak. Past allegations against the company included producing products without a patient specific prescription, failing to follow proper recordkeeping and compounding practices, and instances in which products were implicated in adverse drug events.[4] NECC had recalled products on at least two occasions following adverse events and had been the subject of numerous state and federal complaints and investigations.[5] Ameridose had

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[3] House Committee on Energy and Commerce, Subcommittee on Oversight and Investigations, *Hearing on The Fungal Meningitis Outbreak: Could It Have Been Prevented?* 112th Cong. (Nov. 14, 2012).

[4] *See, e.g.* Food and Drug Administration, *Warning Letter to Barry J. Cadden, NEW-06-07W* (Dec. 4, 2006); Massachusetts Board of Registration in Pharmacy, *Consent Agreement, In the Matter of New England Compounding Center and Barry J. Cadden, Docket Numbers DS-03-055, PH 03-066, and DS 05-040* (Jan. 10, 2006); Massachusetts Department of Public Health, Division of Health Professions Licensure, *Investigation Report: Barry J. Cadden* (Nov. 23, 2004); Massachusetts Department of Public Health, Division of Health Professions Licensure, *Investigation Report: New England Compounding Center and Barry J. Cadden* (Mar. 4, 2004); Food and Drug Administration, *Establishment Inspection Report Attachment, New England Compounding Center* (Feb. 10, 2003); Food and Drug Administration, *Memorandum from Kristina Joyce, Consumer Safety Officer and Mark Lookabaugh, Compliance Officer to Central File* (Feb. 24, 2003).

[5] *See, e.g.* Food and Drug Administration, *Memorandum from Kristina Joyce, Consumer Safety Officer and Mark Lookabaugh, Compliance Officer to Central File* (Feb. 24, 2003); Food and Drug Administration, *Establishment Inspection Report Attachment, New England Compounding Center* (Feb. 10, 2003).

been inspected by state and federal officials on at least five occasions but had never faced an enforcement action prior to the current outbreak.[6] The majority memorandum released on November 12, 2012, and available here contains a detailed description of these interactions.

The November Subcommittee hearing also examined the complex patchwork of laws governing pharmacy compounding. Legal authority over pharmacy compounding has been complicated by court decisions that have cast doubt due to conflicting opinions on FDA's authority to regulate compounders. As a result, compounders have been operating in a regulatory gap between state regulated pharmacies and federally regulated drug manufacturers. At the hearing, FDA Commissioner Hamburg indicated that the agency needed new and clear regulatory authority to address the risks of pharmacy compounding. She testified that "FDA's ability to take action against compounding that exceeds the bounds of traditional pharmacy compounding and poses risks to patients has been hampered by gaps and ambiguities in the law, which have led to legal challenges to FDA's authority to inspect pharmacies and take appropriate enforcement actions. The Administration is committed to working with Congress to address the threat to public health from gaps in authorities for effective oversight of certain compounding practices."[7]

II. REGULATION OF COMPOUNDING PHARMACIES

In 1997, Congress included several new provisions regulating the practice of pharmacy compounding in the Food and Drug Administration Modernization Act (FDAMA) in response to the increasingly common practice of compounders acting as manufacturers.[8] Immediately after the law took effect, compounding pharmacies challenged the advertising and promotion restrictions in Section 503A in federal court.[9] The Ninth Circuit Court of Appeals found that the Section 503A ban on advertising and promotion was an unconstitutional limit on free speech. The Court also found that the unconstitutional provisions could not be severed from Section 503A, thereby voiding the entire section.[10] Subsequently, the Supreme Court agreed that the

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[6] Food and Drug Administration, *Form 483 Issued to Greg Conigliaro,* at 12 (Nov. 9, 2012); Massachusetts Department of Public Health, Division of Health Professions Licensure, Board of Registration in Pharmacy, *Investigative Report, PHA-201-0107 and PHS-2010-0108* (Feb. 10, 2011); Massachusetts Department of Public Health, Division of Health Professions Licensure, Board of Registration in Pharmacy, *Inspection Report: Ameridose, LLC* (Nov. 19, 2008); Food and Drug Administration, *Establishment Inspection Report: Ameridose LLC* (Dec. 7, 2007); Massachusetts Department of Public Health, Division of Health Professions Licensure, Board of Registration in Pharmacy, *Inspection Report: Ameridose, LLC* (July 13, 2006).

[7] House Committee on Energy and Commerce, Subcommittee on Oversight and Investigations, Tesimony of Margaret Hamburg, Commissioner, Food and Drug Aministration, *Hearing on The Fungal Meningitis Outbreak: Could It Have Been Prevented?* 112th Cong. (Nov. 14, 2012).

[8] Pub. L. No.105-115 (1997).

[9] *Western States Medical Center, et al. v. Shalala*, 69 F. Supp. 2d 1288 (D. Nev. 1999).

[10] *Thompson v. Western States Medical Center*, 535 U.S. 357 (2002).

advertising and promotion ban was unconstitutional, but did not comment on whether the unconstitutional provisions could be severed from Section 503A.[11]

FDA issued a Compliance Policy Guide (CPG) in 2002 to help resolve the confusion that occurred following the conflicting court rulings. The CPG outlined the agency's authority over compounders and how it planned to use its enforcement discretion.[12] FDA stated that it would rely heavily on state oversight of compounders and focus its enforcement on compounding pharmacies that were producing large quantities of drugs without valid prescriptions, producing commercially available products, selling drugs wholesale or to third parties for resale, or otherwise violating the new drug, adulteration, or misbranding provisions of the FDCA.[13]

In 2004, compounding pharmacies challenged FDA's authority more broadly, arguing that FDA could not regulate compounded drugs as "new drugs" under the FDCA.[14] In 2008, the Fifth Circuit Court of Appeals found that compounded drugs were "new drugs" and were subject to the FDCA's drug approval, adulteration, and misbranding requirements.[15] The Court disagreed with the Ninth Circuit's view on the severability of Section 503A, effectively reinstating Section 503A within the Fifth Circuit's jurisdiction – Texas, Louisiana, and Mississippi. Throughout the rest of the country not covered by the Fifth or Ninth Circuit decisions, it remains unclear which components of Section 503A remain in force. FDA has therefore continued to exercise its authority under the FDCA in accordance with its 2002 Compliance Policy Guide rather than Section 503A.

III. OPPOSITION TO FDA ACTION BY COMPOUNDING PHARMACISTS

On April 11, 2013, Reps. Waxman, DeGette, Markey, and Dingell released a letter to Chairman Murphy asking him to invite the head of the International Academy of Compounding Pharmacists (IACP) to testify at the hearing. According to the letter:

> A key question for this hearing is why FDA has not acted more forcefully to protect the public from the risks of improperly compounded drugs. At our November hearing, Commissioner Hamburg indicated that weak legislative authority, combined with a series of conflicting court decisions that caused uncertainty as to the validity of the authorizing statute itself, left the agency without adequate authority to act against drug compounders.[16]

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[11] *See* Congressional Research Service, *FDA's Authority to Regulate Drug Compounding: A Legal Analysis* (Oct. 17, 2012).

[12] Food and Drug Administration, *Compliance Policy Guides for FDA Staff and Industry: Section 460.200 Pharmacy Compounding* (May 2002).

[13] *Id.*

[14] *Med. Ctr. Pharmacy v. Mukasey,* 536 F.3d 383 (5th Cir. 2008).

[15] *Id.*

[16] Letter from Rep. Henry A. Waxman, Ranking Member, House Committee on Energy and Commerce, Rep. Diana DeGette, Ranking Member, Subcommittee on Oversight and

Documents provided to the Committee by IACP substantiate Commissioner Hamburg's testimony at the November hearing. These internal documents reveal that for almost two decades, IACP lobbied aggressively and successfully to restrict FDA authority over compounding pharmacies. Even when individuals at the organization's highest levels were aware of significant public health risks from compounding, IACP acted to prevent effective FDA oversight.

Examples of IACP activities highlighted in the letter include IACP's aggressive response to FDA's publication of 2002 guidance specifying agency authority and describing the circumstances by which FDA could take actions against compounders. A draft IACP release on the FDA actions stated:

> IACP believes that FDA has no authority to set national safety standards for pharmacies that are not 'manufacturers.' ... Congress never authorized FDA to act as the National Board of Pharmacy. ... IACP urges FDA to defer to the State Boards of Pharmacy ... for the regulation of compounding practices.[17]

At the same time in 2003, L.D. King, IACP's Executive Director, acknowledged that IACP was aware of problems with drug compounding, writing:

> Today, the risks of pharmacy compounding are well documented. There are multiple cases of adverse affects and documented patient deaths due to pharmacy compounding. There are multiple documented cases of contamination. There are multiple cases of super and sub potent compounded medications dispensed.,[sic] Kansas City Star did an extensive series on pharmacy compounding bringing into question potency, contamination, cases of fraud, lack of education and training, lack of state regulation, technician and pharmacist incompetence, lack of scientific validity, false and misleading claims, and adverse affects to patients. Finally, FDA's study on pharmacy compounding shows an alarming rate of sub-potent medications.[18]

Investigations, House Committee on Energy and Commerce, John D. Dingell, Chairman Emeritus, House Committee on Energy and Commerce Committee, and Edward J. Markey, Ranking Member, House Natural Resources Committee, to Rep. Tim Murphy, Chairman, Oversight and Investigations Subcommittee, Energy and Commerce Committee (Apr. 11, 2013).

[17] International Academy of Compounding Pharmacies, *IACP Publishes Draft Comments Regarding FDA"s Compliance Policy Guide Regarding Compounding Pharmacy (draft)* (July 30, 2002).

[18] *Id.* The materials presented to the Board also indicate that, in response to the FDA study, IACP "commissioned a study to mirror FDA's study of compounded medications and to confirm or refute its results." It is not clear if IACP ever conducted this study or released any information about it.

Despite acknowledging these risks, IACP's legislative strategy focused entirely on eliminating FDA authority. Mr. King wrote that the organization chose not to introduce legislation to clarify that FDA had no legal authority because it "would provide a vehicle for the FDA to amend and get legal authority again."[19] He also wrote that "if FDA or someone else proposed legislation on pharmacy compounding that we are opposed to, it is much easier to kill legislation than to pass it."[20]

IACP has also opposed previous legislative efforts to provide FDA with appropriate authority to regulate drug compounders. In 2007, Senator Edward Kennedy introduced legislation that would have given FDA clear jurisdiction over compounding pharmacies.[21] IACP opposed this legislation. A March 2007 IACP press release titled "Compounding Legislation: It Hurts Everyone," claimed that "Federal legislation that restricts compounding will severely restrict patients' access to proper medicines and doctors' ability to prescribe these medicines."[22]

Chairman Murphy declined to invite IACP to appear at the hearing.

IV. WITNESSES

The following witness has been invited to testify:

Margaret A. Hamburg, M.D.
Commissioner
Food and Drug Administration

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[19] *Id.*

[20] *Id.*

[21] International Academy of Compounding Pharmacists, *Compounding Legislation: It Hurts Everyone* (Mar. 2007).

[22] *Id.*

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MEMORANDUM

April 15, 2013

To: Democratic Members of the Subcommittee on Oversight and Investigations

Fr: Energy and Commerce Committee Democratic Staff

Re: Supplemental Information for Hearing Titled "A Continuing Investigation into the Fungal Meningitis Outbreak and Whether It Could Have Been Prevented"

I. EXECUTIVE SUMMARY

On April 16, 2012, the Subcommittee on Oversight and Investigations will hold a hearing titled "A Continuing Investigation into the Fungal Meningitis Outbreak and Whether It Could Have Been Prevented." In preparation for this hearing, the Committee has received over 27,000 pages of documents from the Food and Drug Administration (FDA) dating from 2002 to 2012. These documents, which were provided in response to a Committee request, reveal several key findings relating to FDA oversight of compounding pharmacies generally and the New England Compounding Center (NECC) in particular. These include:

- FDA has, since 2002, struggled to effectively regulate compounding pharmacies. Although Congress passed legislation in 1997 designed to establish clear rules for when FDA had authority over drug compounders, a series of court decisions that found all or part of this law to be unconstitutional created uncertainty and confusion for FDA, leaving the agency without a coherent policy in place for a decade.

- Beginning in 2009, FDA began to take new steps to develop a coherent and enforceable national policy for drug compounders and drafted a new Compliance Policy Guide (CPG) that would allow the agency to move forward with regulation and oversight. This Compliance Policy Guide appeared to be nearly ready for release in September 2012, immediately before the deadly meningitis outbreak began. But it was never finalized.

- In addition to struggling with the confusion and uncertainty of the court cases governing pharmacy compounding law, FDA officials have, since at least 2002, also been clear that the law itself – the Food and Drug Administration Modernization Act of 1997 (FDAMA)

– had serious flaws that hindered effective regulation of compounding pharmacies and that could best be resolved through new legislation.

- The combination of the flaws in the law itself, the uncertainty created by the court decisions, and the lack of a complete and finalized agency guidance on compounded drugs prevented FDA from effectively acting to address general concerns with compounded pharmacies and specific concerns about the New England Compounding Center.

II. BACKGROUND

Traditional drug compounding involves the mixing or altering of FDA-approved medications by pharmacists to fulfill the special needs of individual patients, such as individuals with allergies or young children who cannot tolerate FDA-approved dosage forms.[1] However, numerous pharmacy compounders have gone beyond the traditional practice of pharmacy compounding, mixing bulk quantities of raw materials to make new drugs, copying FDA-approved products, and selling large volumes of products at the wholesale level.[2] These compounders act more like drug manufacturers than traditional compounding pharmacies. The dual nature of these pharmacies raises questions about appropriate regulatory authority because pharmacies are traditionally regulated at the state level while drug manufacturers are regulated by FDA.[3]

FDA first acted to clarify its regulatory approach to compounding pharmacies in 1992 with the release of a Compliance Policy Guide (CPG).[4] This CPG provided guidance on when the agency would consider taking action against a drug compounder, indicating that FDA would generally defer to state authorities unless compounders were acting in a way more akin to manufacturers – such as when compounders were advertising, compounding in "inordinate amounts," or using commercial-scale manufacturing techniques.

Five years later, Congress passed legislation to specify FDA's authority as part of FDAMA.[5] Section 503A of the law exempted compounded drugs from the other requirements of the Federal Food, Drug, and Cosmetic Act (FDCA), so long as the pharmacy was licensed in a state, made the drug pursuant to a valid prescription for an individual patient, limited interstate

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[1] *See* Lloyd V. Allen, *The Art, Science and Technology of Pharmaceutical Compounding, Chapter 1,* American Pharmacists Association (July 25, 2012).

[2] Office of Representative Edward J. Markey, *Compounding Pharmacies, Compounding Risk* (Oct. 29, 2012).

[3] Congressional Research Service, *FDA's Authority to Regulate Drug Compounding: A Legal Analysis* (Oct. 17, 2012).

[4] Food and Drug Administration, *Compliance Policy Guides for FDA Staff and Industry: Section 460.200 Pharmacy Compounding* (May 2002).

[5] Pub. L. No. 105-115 (1997).

shipments to no more than 5% of the its business, and did not engage in advertising or promotion.[6] Section 503A also states that compounders may not "compound regularly or in inordinate amounts ... any drug products that are essentially copies of a commercially available drug product."[7]

Immediately upon the law's taking effect, compounding pharmacies challenged the advertising and promotion restrictions of the new law in federal court.[8] In February 2001, the Ninth Circuit Court found in the *Western States Medical Center* case that FDAMA's ban on advertising and promotion was an unconstitutional limit on free speech. The Court also found that the unconstitutional provisions could not be severed from section 503A and that the entire section was therefore void.[9] The Supreme Court on April 29, 2002, agreed that the advertising and promotion ban was unconstitutional, but did not comment on the ruling that the unconstitutional provisions could not be severed from section 503A and that the entire section was therefore void.[10]

Following the Supreme Court's ruling, there continued to be confusion over whether FDA retained authority to regulate compounded drugs under section 503A. To resolve this confusion, FDA almost immediately issued a new CPG in May 2002, which outlined the agency's authority over compounders and how it planned to use its enforcement discretion.[11] Much like the 1992 CPG, the 2002 CPG stated that FDA would rely heavily on state oversight of compounders and focus its enforcement on compounding pharmacies that were producing large quantities of drugs without valid prescriptions, producing commercially available products, selling drugs wholesale or to third parties for resale, or otherwise violating the new drug, adulteration, or misbranding provisions of the FDCA.[12]

In 2004, compounding pharmacies challenged FDA's authority more broadly, arguing that FDA could not regulate compounded drugs as "new drugs" under the FDCA.[13] In 2006 and 2008, the district court and subsequently the Fifth Circuit Court of Appeals found that compounded drugs were "new drugs" and were subject to the FDCA's drug approval, adulteration, and misbranding requirements.[14] The circuit court, in what is known as the

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[6] Pub. L. No. 105-115 § 503A (1997).

[7] *Id.*

[8] *Western States Medical Center, et al. v. Shalala,* 69 F. Supp. 2d 1288 (D. Nev. 1999).

[9] *Thompson v. Western States Medical Center,* 535 U.S. 357 (2002).

[10] *See* Congressional Research Service, *FDA's Authority to Regulate Drug Compounding: A Legal Analysis* (Oct. 17, 2012).

[11] Food and Drug Administration, *Compliance Policy Guides for FDA Staff and Industry: Section 460.200 Pharmacy Compounding* (May 2002).

[12] *Id.*

[13] *Medical Center Pharmacy v. Mukasey,* 536 F.3d 383 (5th Cir. 2008).

[14] *Id.*

Medical Center Pharmacy case, also disagreed with the Ninth Circuit's view on the severability of section 503A, effectively reinstating section 503A within the Fifth Circuit's jurisdiction, which covers Texas, Louisiana, and Mississippi.

Throughout the rest of the country not covered by the Fifth or Ninth Circuit decisions, it remains unclear whether the constitutional components of section 503A remain in force.

III. FDA ATTEMPTS TO DEVELOP COMPOUNDING PHARMACY GUIDANCE FROM 2002 TO 2012

A. FDA Response to the 2002 *Western States Medical Center* Decision

In the *Western States Medical Center* decision issued in February 2001, the Ninth Circuit invalidated section 503A of FDAMA. The Supreme Court upheld this decision in April 2002, leaving FDA with difficult decisions on how to regulate compounded drugs.

On May 3, 2002, the Deputy FDA Commissioner, the FDA Chief Counsel, and other top agency officials met. According to a summary of the meeting:

> Section 503A is now invalid in its entirety. FDA will soon need to comment on the effect of this decision on the Agency's programs and policies, specifically, how – and to what extent – the Agency plans to exercise regulatory authority over pharmacy compounding. ...
> FDA is in the process of modifying this [pre-FDAMA] guidance to provide information regarding the Agency's approach to compounding following the Court's decision. ... In order to ensure that legitimate compounding does not fall within the scope of "illegal" activity, legislation may be needed to replace section 503A. FDA is in the process of finalizing a legislative proposal to replace Section 503A. [15]

Included with the materials for this meeting was a presentation that noted the risks of improperly compounded drugs, describing 65 adverse events – including numerous deaths – from "improper compounding processes ... bacterial contamination leading to patient infection ... [and] ingredients with safety and/or efficacy concerns."[16]

In addition, the FDA at this meeting identified significant problems with the implementation of section 503A, citing "loopholes" and problems that hindered enforcement. To resolve these inadequacies, the presentation to the Deputy Commissioner suggested a number of FDA authorities to be clarified in new legislation, including: "No compounding of products

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[15] Food and Drug Administration, *Office of the Commissioner Meeting Executive Summary* (May 3, 2002).

[16] Food and Drug Administration, *Presentation for the Office of the Commissioner by Center for Drug Evaluation and Research: Pharmacy Compounding* (May 3, 2002).

known to be unsafe or withdrawn for safety"; "no copying of commercially available products, medical need"; "No wholesaling"; "Bulk-drug substance requirements"; "limit anticipatory compounding"; and "adverse event reports to states" for compounded drugs.[17]

Within weeks of this meeting, FDA released new guidance in May 2002.[18] The International Academy of Compounding Pharmacies (IACP), the leading compounding pharmacy trade association, immediately criticized the agency for its "haste" in releasing the guidance. In draft comments, IACP stated, "IACP objects to the publication of this guidance without public comment. ... It was both appropriate and feasible for the FDA to allow public comment before publication of a final guidance." [19]

IACP also responded to the substance of FDA authority, stating:

> IACP believes that FDA has no authority to set national safety standards for pharmacies that are not "manufacturers." ... Congress never authorized FDA to act as the National Board of Pharmacy. ... Congress never intended FDA to regulate pharmacies to the same extent as manufacturers. ... IACP urges FDA to defer to the State Boards of Pharmacy... for the regulation of compounding practices.[20]

In response to the concerns of IACP and other stakeholders, FDA said that the agency intended to update the guidance soon in response to stakeholder concerns. In 2003 testimony before Congress, the director of FDA's Center for Drug Evaluation and Research (CDER) stated:

> Although the CPG was immediately effective when it was issued in May 2002, the Agency indicated it would be interested in receiving public comments on the guide. FDA received public comments and is in the process of revising the CPG in response to the comments. The Agency plans to publish a new draft of the CPG and will seek comments on it.[21]

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[17] *Id.*

[18] Food and Drug Administration, *Compliance Policy Guides for FDA Staff and Industry: Section 460.200 Pharmacy Compounding* (May 2002).

[19] International Academy of Compounding Pharmacies, *IACP Publishes Draft Comments Regarding FDA's Compliance Policy Guide Regarding Compounding Pharmacy (draft)* (July 30, 2002).

[20] *Id.*

[21] Senate Committee on Health, Education, Labor, and Pensions, Testimony of Stephen K. Galson, Acting Director, Center for Drug Evaluation and Research, Food and Drug Administration, *Hearing on Federal and State Roles in Pharmacy Compounding and Reconstitution: Exploring the Right Mix to Protect Patients,* 108th Cong. (Oct. 23, 2003) (S. Rept. 90-129) (online at http://www.fda.gov/NewsEvents/Testimony/ucm115010.htm).

Six months later, in a speech before the American Pharmaceutical Association, FDA's CDER Associate Director for Policy reiterated that "we have carefully considered the comments submitted and are revising the guide. We intend to issue a new draft for public comment."[22] She continued, describing the expected changes:

> The new draft CPG is likely to separate and more clearly identify those factors that pertain to distinguishing manufacturing from compounding ... [and] clarify several of the factors, such as those pertaining to industrial scale equipment, on which we received a lot of comments, and what constitutes legitimate compounding for office stock. [23]

She concluded by promising "we will revise the guidance as appropriate and issue a final guidance." [24]

Despite these promises, the FDA during the Bush Administration neither updated nor finalized the guidance.

B. FDA Response to the 2006 and 2008 *Medical Center Pharmacy* Decisions

In August 2006, the district court in the *Medical Center Pharmacy* case determined that although the advertising restrictions in section 503A of FDAMA were unconstitutional, the rest of the section of law was severable and remained in effect. This severability decision was upheld by the Fifth Circuit Court in July 2008.[25]

These court decisions presented FDA with a complicated legal landscape. The agency had published guidance in 2002 that assumed that all of section 503A was no longer applicable and had been in the process of revising that guidance for over five years. But the Fifth Circuit decision meant that section 503A was in effect in that circuit (Louisiana, Mississippi, and Texas); the Ninth Circuit decision meant that section 503A was not in effect in that circuit (Alaska, Arizona, California, Hawaii, Idaho, Montana, Nevada, Oregon, and Washington). The status of the law was uncertain in the rest of the country.

Internal documents provided to the Committee reveal that following the district court's *Medical Center Pharmacy* decision in 2007, the FDA preference was to appeal the severability of section 503A and apply an updated Compliance Policy Guide.

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[22] Speech by Jane Axelrad, Associate Director of Policy, Center for Drug Evaluation and Research, Food and Drug Administration, to the American Pharmaceutical Association, *Pharmacy Compounding: FDA Regulatory Policy* (Mar. 30, 2004).

[23] *Id.*

[24] *Id.*

[25] *Medical Center Pharmacy v. Mukasey,* 536 F.3d 383 (5th Cir. 2008).

FDA internal documents from a January 2007 briefing of the Commissioner describe the agency preference, noting that "the purpose of the meeting is for CDER to brief the Commissioner on the importance of appealing the recent ruling in the *Medical Center Pharmacy* case that an advertising ban in Section 503A ... can be severed from the rest of Section 503A, leaving that provision in effect."[26] There were multiple rationales for this preference:

> [A]s a regulatory tool, Section 503A has critical gaps. ... Returning to Section 503A also will require agency resources that are not available. ... This would effectively drain the compounding program's available resources, bringing consumer protection in this area to a standstill. In addition, reviving Section 503A will create a regulatory muddle. There will be split of authority between the Ninth Circuit ... and those parts of the country in which Section 503A is in effect. [27]

The meeting notes concluded that the "better alternative is to continue to regulate this area, as FDA has for the last half-decade, through a compounding CPG. ... The revised CPG is now complete."[28]

An additional document prepared for the Commissioner's meeting describes the problems with section 503A, and the enforcement difficulties it would present for FDA in several key areas where the agency had concerns about compounded drugs, such as large scale compounding of unsafe drugs, fraudulent drugs, or copies of commercially available drugs; drugs that were withdrawn from the market; and contaminated compounded drugs.[29]

A power-point presentation that was prepared in conjunction with the Commissioner's meeting provided additional detail. It stated, "The revised CPG is an effective enforcement tool. ... The revised CPG responds to compounders' and Congress's concerns."[30] Under "Next Steps," the presentation listed "Publish the draft revised CPG."[31]

Despite this recommendation, FDA did not finalize the CPG prior to the end of the Bush Administration.

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[26] Food and Drug Administration, *Office of the Commissioner Meeting Executive Summary* (Jan. 12, 2007).

[27] *Id.*

[28] *Id.*

[29] Food and Drug Administration, *Cases CPG vs. 503A(2)* (Jan. 19, 2007).

[30] Briefing by Steven Silverman, Assistant Director, Office of Compliance, Center for Drug Evaluation and Research, Food and Drug Administration, *Compounded Human Drugs Briefing* (Jan. 12, 2007).

[31] *Id.*

C. FDA Action from 2009 to Present

By the time the Obama Administration entered office in January 2009, FDA guidance and law regarding compounding pharmacies had been governed by confusion and uncertainty for almost seven years.

In May 2009, top FDA officials met to resolve these problems. The Director and Assistant Director of CDER's Office of Compliance met with the Acting FDA Commissioner "to request the Acting Commissioner's support for a plan to clarify FDA's authority over compounded drugs in the aftermath of two court decisions. ... In addition, we seek the Acting Commissioner's support for pursuing legislative changes to section 503A to expand FDA's authority over compounded human drugs."[32]

The meeting summary noted that "unregulated compounding raises significant public health concerns. ... FDA has seen numerous examples of serious patient injury and death caused by improper compounding." [33]

In order to rectify those problems, FDA was presented with three options: (1) "Apply section 503A in the Fifth Circuit and the compounding CPG elsewhere"; (2) "Apply section 503A nationwide except in the Ninth Circuit ... [i]n the Ninth Circuit, exercise enforcement discretion to allow compounding that ... would satisfy section 503A"; or (3) "Seek legislation amending section 503A and otherwise enhancing FDA's oversight of compounded drugs (*e.g.*, through records-inspection authority and mandatory adverse event reporting). While these efforts are underway, apply those parts of section 503A that do not require rulemaking or consultation with an advisory committee."[34] Option (3) was the "recommended" option.[35]

When recommending option (3), FDA officials said the advantage is that the "approach would fix critical flaws in section 503A."[36] The disadvantage centered on the likely opposition:

> The legislative process will be time and resource intensive and the compounding community will actively oppose the changes that we seek. They have a very effective grass-roots organization that will make it difficult for us to achieve our legislative ends. We cannot know if the result of our efforts will be better law than section 503A in its current form. [37]

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[32] Food and Drug Administration, *Office of the Commissioner Meeting Executive Summary* (May 12, 2009).

[33] *Id.*

[34] *Id.*

[35] *Id.*

[36] *Id.*

[37] *Id.*

FDA officials appeared to take a hybrid approach, applying section 503A nationwide while working on legislation to fix the deficiencies in section 503A. A July 2009 e-mail from the Acting Chief Counsel at FDA noted that the "[p]lan is 503A except in 9th Circuit."[38]

A July 5, 2012, memo from a FDA Associate Chief Counsel to the FDA Chief Counsel looked back and described this decision as being driven by the Department of Justice assessment of the legal arguments at play in 2009. According to the memo:

> The Department of Justice, however, recommended to the solicitor general that the [*Medical Center Pharmacy*] decision not be appealed. DOJ believed that the argument in favor of severability is considerably stronger. ... To address the agency's concerns about applying a uniform policy throughout the country, DOJ recommended that the agency implement section 503A nationwide. ... In 2009, [senior FDA officials] met ... to discuss the agency's preferred approach for regulating compounding in light of the developments described above. It was decided that the agency would enforce section 503A nationwide except for in the 9th Circuit. It's not clear whether the agency intended to continue to use the 2002 CPG for the 9th Circuit or to develop a new one. In any case, CDER has decided to issue a new CPG that would announce our intention to implement 503A except for the 9th circuit, where the agency will exercise its enforcement discretion consistent with the provision in 503A.[39]

After the 2009 decision, FDA moved forward with implementing this decision. By November 2010, the draft guidance was prepared. A memo accompanying this draft was sent to "FDA Clearance Officials" on November 1, 2010. It stated:

> The primary purpose of this Guidance is to explain how FDA will enforce Section 503A in light of the split in the Circuit Courts and the Supreme Court's silence concerning the severability of the advertising prohibitions of section 503A from the rest of section 503A. It announces that FDA intends to apply section 503A nationwide except in the Ninth Circuit, where the Agency will exercise enforcement discretion regarding compounding that satisfies the criteria articulated in section 503A and this Guidance.[40]

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[38] E-mail from Michael Landa, Acting Chief Counsel, Office of General Counsel, Food and Drug Administration, to Kevin Fain et al. (July 29, 2009).

[39] Memorandum from Nicholas Beshara, Associate Chief Counsel, Food and Drug Administration, to Elizabeth Dickinson, Chief Counsel, Food and Drug Administration, *Application of Section 503A* (July 2012).

[40] Memorandum from the Staff of the Office of Compliance, Center for Drug Evaluation and Research, Food and Drug Administration, to Food and Drug Administration Clearance Officials, *Draft Guidance on Compounding of Human Drugs Under Section 503A of the Federal Food, Drug, and Cosmetic Act – Compliance Policy Guide* (Nov. 1, 2010).

The accompanying draft guidance document included a section on "considerations that could result in enforcement action." This section described a number of actions that could result in FDA enforcement actions against compounders, including "producing drugs in anticipation of receiving prescriptions except in limited quantities ... producing drugs for interstate shipment ... producing drugs for resale through wholesale distributors ... [and] producing drugs that violate statutory requirements."[41]

By April 2011, FDA appeared to have completed two related guidance documents in draft form, referred to as the Outsourcing/Centralized Hospital Admixture/Office Stock Guidance and the Sterile Compounding Guidance, and prepared these to move towards final clearance in conjunction with the compounding CPG.[42]

In October 2011, another memo to CDER Clearing Officials from FDA's Office of Unapproved Drugs and Labeling Compliance described the timeline for FDA actions with the proposed guidance, noting that "[w]e plan to issue the revised Guidance to Industry for Comment by December 2011."[43]

This memo also made clear the need for stronger legislation to address the risks of drug compounding. The memo noted:[44]

> We will propose legislative changes for the following points, in order of importance:
>
> - Removal of provision 503A(c) for advertising and promotion
> - Clarify inspectional authority under 704(a)
> - Recall authority for compounded drug products
> - Clarification for the applicability for use of approved "human" drug in 503A

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[41] Food and Drug Administration, *Unreleased Draft Guidance for FDA Staff and Industry, Compounding of Human Drugs Under Section 503A of the Federal Food, Drug, and Cosmetic Act* (2010).

[42] Memorandum from the Staff of the Office of Compliance, Center for Drug Evaluation and Research, Food and Drug Administration, to Food and Drug Administration Clearance Officials, *Clearance Memo for Three Compounding Guidances to Clear and Publish Together: (1) Compounding of Human Drugs Under Section 503A of the Federal Food, Drug, and Cosmetic Act; (2) Pharmacies That Compound Drugs Without Prescriptions for Medical Facilities; and (3) Good Pharmacy Compounding Practices for Sterile Drug Products* (Apr. 1, 2011).

[43] Memorandum from Office of Unapproved Drugs and Labeling Compliance, Food and Drug Administration, to Center for Drug Evaluation and Research Clearing Officials, *Rationale for 503A Policy and Regulatory Strategy* (Oct. 4, 2011).

[44] *Id.*

- ADE [Adverse Drug Event] reporting or inclusion for FAR [Field Alert Reports]

The same memo described FDA's suspension of compounding facilities inspections until completion of the CPG. It stated: "Currently we have suspended inspections of compounding facilities. We will reinstate proactive inspections based on a risk model three to six months after the finalization of the guidance to the industry."[45]

The draft guidance continued to move through the agency. In February 2012, an FDA memo indicates that "CDER Center Director staff asked CDER Office of Compliance to revise the draft."[46] In a May 17, 2012, e-mail, FDA's Director of the Division of Compliance Policy wrote, "This CPG has cleared all necessary offices, although I am still catching up on signatures ... The working group has an ambitious deadline and the task is important to the ACRA [Associate Commissioner for Regulatory Affairs] ... as well as the Commissioner."[47] An August 2012 memo noted, "As of July 2012, this CPG is undergoing final clearance with anticipated publication in September 2012."[48]

By September 2012, as contaminated drugs from NECC began to cause the meningitis outbreak, FDA officials appeared to be close to releasing this new guidance. A September 17, 2012, meeting was held to "initiate collaboration between CDER/OC and ORA field experts on implementation of the new CPG for compounding pharmacies (in sign-off)."[49] And an October

[45] Memorandum from Office of Unapproved Drugs and Labeling Compliance, Food and Drug Administration, to Center for Drug Evaluation and Research Clearing Officials, *Rationale for 503A Policy and Regulatory Strategy* (Oct. 4, 2011).

[46] Memorandum from Director, Division of Compliance Policy, Office of Enforcement, Food and Drug Administration, to Armanda Zamora, Food and Drug Administration, *CPG 460.200 Pharmacy Compounding of Human Drug Products under 503A of the FFDCA* (Feb. 24, 2012).

[47] E-mail from Andrea Chamblee, Director, Division of Compliance Policy, Food and Drug Administration, to Armando Zamora, Food and Drug Administration, and Kara Lynch, Food and Drug Administration (May 17, 2012).

[48] Memorandum from Carol J. Bennett, Acting Assistant Commissioner for Compliance Policy, Food and Drug Administration, et al. to Dara Corrigan, Associate Commissioner for Regulatory Affairs, Food and Drug Administration, and Howard Sklamberg, Deputy Associate Commissioner for Regulatory Affairs, Food and Drug Administration, *Compounding Pharmacies – Enforcement Issues* (Aug. 28, 2012).

[49] Food and Drug Administration, *CDER/ORA Compounding Pharmacy Compliance Policy* (Sept. 17, 2012).

2012 memo to FDA's Chief Counsel described in detail the key enforcement and interpretation issues contained in the upcoming CPG.[50]

FDA was not able to complete the draft CPG before the meningitis outbreak. Even if it had, it is not clear what effect the guidance would have had. As noted in FDA documents since 2002, there were major flaws in the law that hindered effective enforcement.

IV. EFFECT OF UNCERTAINTY ON REGULATION OF NECC AND RELATED FIRMS

One unfortunate consequence of the decade of legal and regulatory uncertainty regarding compounding pharmacies was to delay or prevent FDA action on NECC and related companies on numerous occasions from 2006 through 2012.

Internal agency correspondence from August 2006 indicates that the failure of the Bush Administration to finalize the compounding CPG was delaying and hindering agency enforcement actions against compounding pharmacies, including NECC. In an e-mail sent in August 2006, the Assistant Director of CDER's Office of Compliance wrote to a counsel in the FDA Office of Chief Counsel expressing frustration with delays in issuing Warning Letters to drug compounders. He wrote, "I'm very frustrated that we still don't have a decision from your office about these warning letters. ... For these letters to still be pending at this late date, especially given these extraordinary and unusual measures, is troubling."[51]

E-mails later that month indicate that inactivity and indecision on a revised CPG were responsible for the delays. On August 10, 2006, the Director of FDA's Office of Compliance wrote to FDA's Deputy Commissioner for Medical and Scientific Affairs, expressing concern about delays in sending warning letters to drug compounders. She wrote:

> We have been told by OGC [Office of General Counsel] that they will clear 5 pending letters soon. But, even if that happens, thirteen will remain pending. Most crucially, our revised draft compounding CPG remains in limbo at OGC, and we are under constant pressure from Congress, the Small Business Administration, and others to get that on the street. Even if the draft is not perfect, it's better than the current state of affairs.[52]

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[50] Memorandum from Nicholas Beshara, Associate Chief Counsel, Food and Drug Administration, to Elizabeth Dickinson, Chief Counsel, Food and Drug Administration, *Draft Compounding CPG Announcing Enforcement of Section 503A of the FDCA* (Oct. 2, 2012).

[51] E-mail from Steven Silverman, Food and Drug Administration, to William McConagha, Food and Drug Administration (Aug. 2, 2006).

[52] E-mail from Deb Autor, Food and Drug Administration, to Scott Gottlieb, Food and Drug Administration, Kathleen Anderson, Food and Drug Administration, Samia R. Nasr, Food and Drug Administration, and Steven Silverman, Food and Drug Administration (Aug. 10, 2006).

Among the letters flagged in the e-mail as being delayed was a draft Warning Letter to NECC.

Two days later, the Associate Director for Policy at CDER, who was copied on the e-mail, replied, "I talked to [an FDA senior counsel] and he thinks we will get the CPG out of OGC soon."[53]

The Warning Letter to NECC referred to in this e-mail was not sent for another four months, until December 2006. After NECC replied to the Warning Letter in January 2007, it took FDA almost two more years to send a response to NECC, in October 2008. FDA conducted no further investigations of NECC prior to the meningitis outbreak.

In the 2008 to 2009 time period, FDA's difficulty in resolving the conflicting court opinions appeared to have prevented the agency from sending a formal warning letter after finding problems at Ameridose, a sister company that shared ownership with NECC. FDA conducted several inspections of Ameridose in 2008, identifying a series of problems with the firm's practices. In October 2008, an official in the New England Office of the FDA recommended and drafted a Warning Letter to be sent to NECC based on this inspection.[54] However, according to a December 2009 e-mail from the New England District Director, "the [Warning Letter] was put on hold by OCC [Office of Chief Counsel] on 9/1/09 due to conflicting court rulings related to Pharmacy Compounding. CDER did not proceed with the issuance of this WL."[55]

Later in the e-mail, the District Director wrote that "CDER will be issuing an assignment for Ameridose after an outsourcing guidance document has been cleared through CDER ... I'm not sure when this will be but it should be soon." [56]

FDA did inspect Ameridose in 2010 in conjunction with the Massachusetts Board of Pharmacy.[57] In July 2011, FDA officials had another discussion about a possible inspection of Ameridose in part in response to problems identified during the 2010 inspection. A senior counsel in the FDA Office of General Counsel wrote to the agency's Deputy General Counsel for Litigation:

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[53] E-mail from Deborah Autor, Food and Drug Administration, to Jane Axelrad, Food and Drug Administration (Aug. 10, 2006).

[54] Food and Drug Administration, *Draft Warning Letter No. 2008-NEW-DO* (2008).

[55] E-mail from Mutahar Shamsi, Director, Compliance Branch, Food and Drug Administration, to William Blovin et al. (Dec. 8, 2009).

[56] *Id.*

[57] Food and Drug Administration, *Establishment Inspection Report of Ameridose LLC* (July 7, 2008).

> I talked to you briefly about CDER's desire to inspect a pharmacy outsourcer called Ameridose. ... At the time, you were reluctant to move in this direction until the CDER guidances issue. ... At the internal meeting we had, I conveyed your view that we should not go an[d] inspect the firm until the 503A FR notice and outsourcer guidance (collectively "guidance") issue. *CDER would nonetheless like to go forward with the inspection* because they have concerns about the firm's operations and they do not wish to wait to address those concerns until the guidance issues, the agency receives comments and puts the guidance in final, and then an appropriate amount of time passes so that we can inspect against the criteria in the guidance.[58]
>
> The Deputy General Counsel replied:
>
> It is CDER's call, but if the problems are serious safety issues, why would we only issue a WL? Why not seize? ...
>
> My concern was that ... we issue a WL under one legal theory and then either do nothing til we issue the guidance (+@6 months) which apparently will be forever or, as you note below, put another nail in our consistent policy coffin by reinspecting and filing under a pre-guidance theory.
>
> It is disconcerting to say the least that we are regulating for so long without having adopted a thought out and transparent policy.[59]

In reply, the FDA attorney stated, "I don't think we know enough right now to know whether there are current serious problems that raise real safety issues. We'll have to make that assessment after the inspection and then act appropriately."[60]

During this time period, FDA also received additional reports of problems at NECC. In May 2011, Colorado Board of Pharmacy officials reported problems with NECC to FDA. One year later, in July 2012, this information was sent to the FDA Compliance Officer handling NECC. His reply to this e-mail indicates that the FDA would consider an inspection of NECC after the FDA released the CPG for compounders, writing "[b]ased on past conversations that we

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[58] E-mail from Paige Taylor, Senior Counsel, Office of General Counsel, Food and Drug Administration, to Eric Blumberg, former Deputy Chief Counsel, Food and Drug Administration (July 6, 2011).

[59] E-mail from Eric Blumberg, former Deputy Chief Counsel, Food and Drug Administration, to Paige Taylor, Senior Counsel, Office of General Counsel, Food and Drug Administration (July 6, 2011).

[60] E-mail from Paige Taylor, Senior Counsel, Office of General Counsel, Food and Drug Administration, to Eric Blumberg, former Deputy Chief Counsel, Food and Drug Administration (July 6, 2009).

may start enforcing compounding pharmacies at the end of this year do you want us to wait until you issue an assignment to go to the firm?"[61]

V. CONCLUSION

Tomorrow, the Subcommittee on Oversight and Investigations will receive testimony from FDA Commissioner Margaret Hamburg. She will be able to address the topics detailed in this memorandum.

[61]E-mail from Bruce Ota, Compliance Office, New England District, Food and Drug Administration, to Lisa Tung, Food and Drug Administration, and Pamela Lee, Food and Drug Administration (July 17, 2012).

THE COMMITTEE ON ENERGY AND COMMERCE

Memorandum

April 14, 2013

TO: Members, Subcommittee on Oversight and Investigations

FROM: Subcommittee on Oversight and Investigations Staff

RE: Hearing on "A Continuing Investigation into the Fungal Meningitis Outbreak and Whether It Could Have Been Prevented"

On Tuesday, April 16, 2013, at 10:00 a.m. in room 2123 of the Rayburn House Office Building, the Subcommittee on Oversight and Investigations will hold a hearing entitled "A Continuing Investigation into the Fungal Meningitis Outbreak and Whether It Could Have Been Prevented."

This hearing is a continuation of the Subcommittee's examination of the facts surrounding the 2012 outbreak of fungal meningitis caused by contaminated steroids made and distributed by the New England Compounding Center (NECC) in Framingham, Massachusetts. As was the intent of the first hearing on November 14, 2012, the Subcommittee will examine the Food and Drug Administration's (FDA) history with NECC and its sister company, Ameridose, to determine whether this tragedy could have been prevented had the agency taken action sooner.

I. WITNESS

The Honorable Margaret A. Hamburg, MD
Commissioner
U.S. Food and Drug Administration (FDA)

II. BACKGROUND

As of April 2013, 53 people have died and almost 700 others have been stricken with meningitis or other serious fungal infections after having received contaminated injections of methylprednisolone acetate—a compounded steroid solution, 17,000 vials of which had been made by NECC and shipped to health care facilities across the country. This outbreak ranks as one of the worst public health crises associated with contaminated drugs in the history of the United States.

In early October 2012, bipartisan Committee staff received briefings from FDA and the Centers for Disease Control and Prevention (CDC), as well as from the Massachusetts Department of Public Health (MDPH), to determine how something like this could happen. Knowing that FDA had sent a Warning Letter to NECC in December 2006, on October 12, 2012,

bipartisan Committee staff requested a timeline documenting the agency's past interactions with NECC and Ameridose in order to gain a better understanding of their inspectional history and any related actions FDA had taken. This timeline was produced to the Committee on January 4, 2013, and is attached to this memorandum (see Attachment A). Prior to its November 14, 2012, hearing, the Subcommittee did not know the full extent of FDA's history with NECC leading up to the meningitis outbreak or whether the agency had received recent complaints about NECC and/or Ameridose that raised questions about the nature of their operations and the safety of their products. Neither Commissioner Hamburg's testimony nor the timeline FDA subsequently produced provided much detail about any complaints, warnings, or reports FDA received about these companies.

Following the November 2012 hearing, based on Commissioner Hamburg's testimony, the Committee sent a letter to FDA requesting memoranda and briefing materials related to FDA's assessment of its authority over compounding to determine how this influenced agency decision-making with respect to NECC and Ameridose. Over the course of the next two months, the Committee pressed FDA to produce its documents related to the fungal meningitis outbreak. On February 1, 2013, the Committee sent Commissioner Hamburg another letter regarding its document requests. In that letter, Committee Chairman Upton and Oversight Subcommittee Chairman Murphy stated that if FDA did not produce all responsive documents by February 25, 2013, the Committee would issue a subpoena. FDA finally completed its production on March 21, 2013.

Documents produced by FDA establish the following facts about the agency's history with NECC and its sister company, Ameridose:

1. FDA has known for years that NECC and Ameridose were significantly engaged in drug manufacturing activities and operating well outside the bounds of traditional pharmacy compounding.

2. FDA has also received a litany of complaints about NECC and Ameridose, a number of which directly involved the safety and sterility of the companies' products.

3. Information received by FDA about NECC and Ameridose, including complaints about the safety and sterility of their products, was not shared with State regulators.

Since the November 2012 hearing, FDA held a public meeting with the State pharmacy boards to discuss ways to facilitate increased communication and develop a framework to ensure adequate oversight. FDA has since inspected almost 50 compounding facilities. The majority of these firms were selected for inspection based on their production of sterile injectable drug products alone; however, FDA had received complaints associated with the products and practices of a number of the companies targeted. As with NECC and Ameridose, FDA had already documented serious violations of the Food, Drug, and Cosmetic Act (FDCA) at several

of these very facilities. Based on these recent inspections, FDA has issued Form 483s[1] to approximately 30 of the facilities and posted the documents on the agency's website—an additional step the agency has not typically taken in the past.

III. ISSUES

- Why did FDA decide not to reinspect NECC after stating that it would do so in a Warning Letter to the company in December 2006 and then again in related correspondence two years later?
- What did FDA know about the relationship between NECC and Ameridose?
- How did FDA protect patient safety as it grappled with its authority over drug compounding?
- What did FDA know about the nature and scope of the companies' operations and the safety of their products?
- How did such knowledge influence the agency's assessment of whether NECC and/or Ameridose should be considered a traditional compounding pharmacy versus a drug manufacturer?

IV. STAFF CONTACTS

If you have any questions regarding this hearing, please contact Karen Christian or John Stone with the Subcommittee on Oversight and Investigations at (202) 225-2927.

[1] FDA issues a Form 483 at the end of an inspection when the investigators believe that the observed conditions or practices, in their judgment, may indicate violations of the FDCA or any related regulations. FDA has stated that its goal in issuing a 483 is to have the company act quickly to correct potential violations. The FDA considers the 483 along with an Establishment Inspection Report (EIR), prepared by FDA investigators, and any other information, including any responses received from the company, to determine whether further action is appropriate.

FRED UPTON, MICHIGAN
CHAIRMAN

HENRY A. WAXMAN, CALIFORNIA
RANKING MEMBER

ONE HUNDRED THIRTEENTH CONGRESS

Congress of the United States
House of Representatives
COMMITTEE ON ENERGY AND COMMERCE
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April 11, 2013

The Honorable Tim Murphy
Chairman
Subcommittee on Oversight and Investigations
Committee on Energy and Commerce
2125 Rayburn House Office Building
Washington, D.C. 20515

Dear Chairman Murphy:

Next week, the Subcommittee will be holding our second hearing into the deadly meningitis outbreak caused by contaminated injectable drugs from the New England Compounding Center (NECC). You have invited Margaret Hamburg, the Food and Drug Administration (FDA) Commissioner to testify at this hearing. We think you should also invite the head of the International Academy of Compounding Pharmacists (IACP), the national organization representing compounding pharmacists.

A key question for this hearing is why FDA has not acted more forcefully to protect the public from the risks of improperly compounded drugs. At our November hearing, Commissioner Hamburg indicated that weak legislative authority, combined with a series of conflicting court decisions that caused uncertainty as to the validity of the authorizing statute itself, left the agency without adequate authority to act against drug compounders.[1]

Documents provided to the Committee by IACP substantiate Commissioner Hamburg's testimony. These documents reveal that for almost two decades, IACP lobbied aggressively and successfully to restrict FDA authority over compounding pharmacies. Even when individuals at the organization's highest levels were aware of significant public health risks from compounding, IACP acted to prevent effective FDA oversight.

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[1] House Committee on Energy and Commerce, Subcommittee on Oversight & Investigations, *Hearing on The Fungal Meningitis Outbreak: Could it Have Been Prevented?* 112th Cong. (Nov. 14, 2012).

IACP's past efforts and statements stand in sharp contrast to the organization's recent statements that FDA's authority in this area is "clear, direct, and certain."[2] The information contained in IACP's documents helps explain why FDA would have had difficulty acting to regulate compounding pharmacies. Most importantly, the documents show why legislation that gives FDA clear authority to regulate compounding pharmacies is now necessary.

We are thus requesting that you invite a representative from IACP to the April 16 hearing so we can understand the organization's past actions and current views on FDA authority over compounding pharmacies.

Introduction

In September 2012, officials in Tennessee identified the first of hundreds of cases of fungal meningitis in patients who had received contaminated injectable products made and distributed by a Massachusetts based drug compounder. To date, 733 individuals have contracted fungal meningitis, and 53 have died from injections of preservative-free methylprednisolone acetate compounded by the New England Compounding Center.[3] Prior to this incident, both the Massachusetts State Board of Pharmacy and FDA had inspected the facility and identified numerous issues with its procedures and practices. Despite this history, the drug compounding company was allowed to continue to distribute products without significant disruption.

On November 14, 2012, the Committee on Energy and Commerce's Subcommittee on Oversight and Investigations held a hearing on the fungal meningitis outbreak.[4] During the hearing, FDA Commissioner Dr. Margaret Hamburg stated that FDA's ability to regulate and oversee compounding facilities, like NECC, was often limited because legal decisions had created "enormous lack of clarity" regarding FDA's authority over drug compounding.

On December 7, 2012, members of the Committee sent a letter to IACP requesting information on allegations that IACP "tutored pharmacists on how to sidestep [FDA] requests"

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[2] International Academy of Compounding Pharmacists, *FDA Authority is Clear, Direct, and Certain* (Nov. 20, 2012) (online at www.prnewswire.com/news-releases/iacp-fda-authority-is-clear-direct-and-certain-180216081.html) (press release).

[3] Centers for Disease Control and Prevention, *Multistate Fungal Meningitis Outbreak – Current Case Count* (Apr. 8, 2012) (online at www.cdc.gov/hai/outbreaks/meningitis-map.html).

[4] House Committee on Energy and Commerce, *Subcommittee on Oversight & Investigations, Hearing on The Fungal Meningitis Outbreak: Could it Have Been Prevented?* 112th Cong. (Nov. 14, 2012).

for samples related to the agency's assessment of the quality of compounded drugs.[5] In response, IACP briefed Committee staff on these allegations and provided over 3,000 pages of documents relating to their work on behalf of their member pharmacies. Committee investigators reviewed the documents provided to the Committee by IACP. They also reviewed public statements by IACP and its member drug compounding companies and legal and regulatory filings submitted by these organizations. These documents reveal that for almost two decades, IACP has aggressively acted to limit FDA authority over compounding pharmacies.

IACP's Efforts to Block FDA Regulation of Compounding Pharmacies

One IACP document, an undated internal history entitled "Compounders on Capitol Hill," describes efforts beginning in 1995 to "enact legislation to protect our right to compound."[6] This legislation ultimately was incorporated into the Food and Drug Administration Modernization Act of 1997 (FDAMA), which FDA has identified as a key reason the agency's authority is uncertain. The same IACP internal history reveals that in 1999, almost immediately after FDA commenced implementing this new law, IACP began to lobby Congress to further rein in the agency, citing FDA "overreach" in efforts to address limits on drug compounders.[7]

When FDA published a draft Compliance Policy Guide (CPG) in 2002 specifying agency authority and describing when FDA could take actions against compounders, IACP responded aggressively. A draft release on the FDA actions stated:

> IACP believes that FDA has no authority to set national safety standards for pharmacies that are not 'manufacturers.' ... Congress never authorized FDA to act as the National Board of Pharmacy. ... IACP urges FDA to defer to the State Boards of Pharmacy ... for the regulation of compounding practices.[8]

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[5] Letter from the Honorable Fred Upton, Chairman, Committee on Energy and Commerce, and the Honorable Henry A. Waxman, Ranking Member, Committee on Energy and Commerce, et. al. to Mr. Scott Karolchyk, President, Board of Directors, International Academy of Compounding Pharmacists (Dec. 7, 2012).

[6] International Academy of Compounding Pharmacists, *Compounders on Capitol Hill: A History of Affecting Change*, at 38 (2008).

[7] *Id.*

[8] International Academy of Compounding Pharmacists, *IACP Publishes Draft Comments Regarding FDA's Compliance Policy Guide Regarding Compounding Pharmacy* (Jul. 30, 2002).

IACP's public affairs counsel later told the organization that "CPGs by their very nature do not have the force of law. As stated in its preamble, it is only the 'current thinking' of the agency and 'does not operate to bind FDA or the public.'"[9]

At a July 2003 board meeting, the IACP's Secretary "expressed his intention of launching a full-scale assault on FDA" in response to agency actions on veterinary compounding.[10]

At the same time – amid uncertainty over FDA actions and court decisions – L.D. King, IACP's Executive Director, wrote to the Board of Directors that "[b]ecause of the Supreme Court case FDA does not enjoy clear legal authority over pharmacy compounding."[11] In his memorandum to the board, Mr. King acknowledged that IACP was aware of problems with drug compounding, writing:

> Today, the risks of pharmacy compounding are well documented. There are multiple cases of adverse affects and documented patient deaths due to pharmacy compounding. There are multiple documented cases of contamination. There are multiple cases of super and sub potent compounded medications dispensed.,[sic] Kansas City Star did an extensive series on pharmacy compounding bringing into question potency, contamination, cases of fraud, lack of education and training, lack of state regulation, technician and pharmacist incompetence, lack of scientific validity, false and misleading claims, and adverse affects to patients. Finally, FDA's study on pharmacy compounding shows an alarming rate of sub-potent medications.[12]

Despite acknowledging these risks, IACP's legislative strategy focused entirely on eliminating FDA authority. Mr. King wrote that the organization chose not to introduce

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[9] E-mail from James W. Rock, Parry, Romani, DeConcini, & Symms, to Jennifer Goodrum, International Academy of Compounding Pharmacists, L.D. King, International Academy of Compounding Pharmacists, Tara McCarthy, International Academy of Compounding Pharmacists, and Sarah Dodge, International Academy of Compounding Pharmacists (Nov. 11, 2008).

[10] International Academy of Compounding Pharmacists, *Board Meeting Minutes* (June 7, 2003).

[11] Memorandum from L.D. King, Executive Director, International Academy of Compounding Pharmacists, to International Academy of Compounding Pharmacists Board of Directors (Oct. 8, 2003).

[12] *Id.* The materials presented to the Board also indicate that, in response to the FDA study, IACP "commissioned a study to mirror FDA's study of compounded medications and to confirm or refute its results." It is not clear if IACP ever conducted this study or released any information about it.

legislation to clarify that FDA had no legal authority because it "would provide a vehicle for the FDA to amend and get legal authority again."[13] He also wrote that "if FDA or someone else proposed legislation on pharmacy compounding that we are opposed to, it is much easier to kill legislation than to pass it."[14]

An August 2005 "Public Affairs Strategy Memo" prepared by IACP's public affairs firm and sent to the IACP Executive Director identified "maintain[ing] states' ultimate authority over compounding" as a top goal for the organization.[15] To achieve this goal, the memo called for IACP to "develop greater support on Capitol Hill," including the possibility of "reviving [legislation] reiterating that compounding falls under state authority."[16] This memo also recommended that IACP "Mobilize a states' rights and pro-business campaign," led by "states' rights advocates … small business advocates … [and] conservative think tanks like Heritage, Cato and AEI."[17]

IACP documents from 2006 describe an effort to "proselytize the role of the state boards of pharmacy as the appropriate entity to regulate the profession, as opposed to FDA or another body."[18]

In 2007, Senator Edward Kennedy introduced legislation that would have given FDA clear jurisdiction over compounding pharmacies.[19] IACP opposed this legislation. A March 2007 IACP press release titled "Compounding Legislation: It Hurts Everyone," claimed that "Federal legislation that restricts compounding will severely restrict patients' access to proper medicines and doctors' ability to prescribe these medicines."[20]

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[13] *Id.*

[14] *Id.*

[15] Memorandum from Bob Chlopak, Josh Wonderoff, Tammy Gordon, Chlopak, Leonard, Schecter, and Associates, to L.D. King and Jennifer Goodrum, International Academy of Compounding Pharmacists, at 2675 (Aug. 9, 2005).

[16] *Id.*

[17] *Id.*

[18] International Academy of Compounding Pharmacists, *Government and Regulatory Affairs – Consent Agenda Items* (Oct. 11, 2006).

[19] International Academy of Compounding Pharmacists, *Compounding Legislation: It Hurts Everyone* (Mar. 2007).

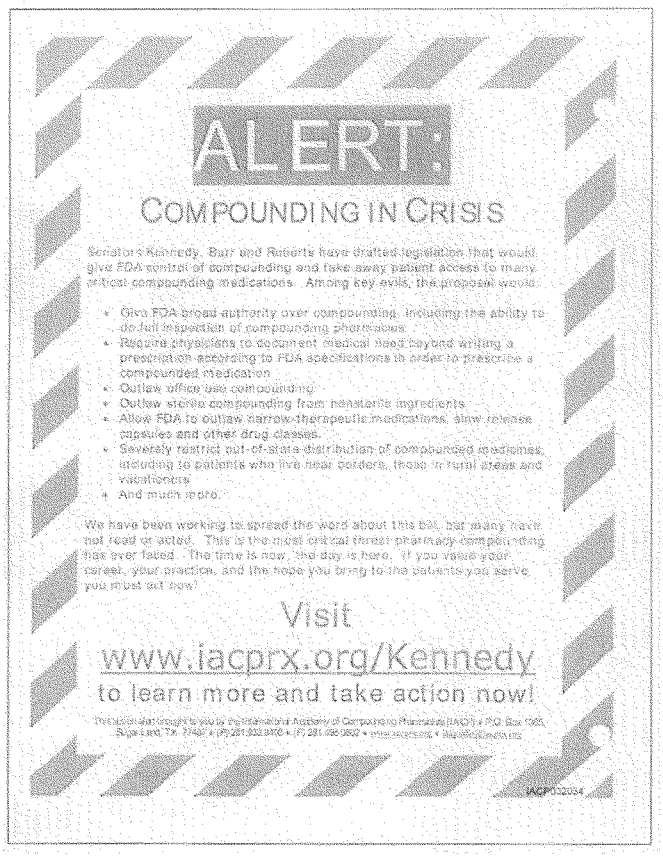
[20] *Id.*

To marshal opposition to this legislation, IACP sent an alert to its members. The title of this alert is "Compounding in Crisis."[21] According to the alert:

> This is the most critical threat pharmacy compounding has ever faced. The time is now, the day is here. If you value your career, your practice, and the hope you bring to patients you serve, you must act now![22]

[21] International Academy of Compounding Pharmacists. *Compounding In Crisis* (2007).

[22] *Id.*



IACP called for opposition to the legislation, stating that "FDA has proven itself to be an overly aggressive regulator of compounding and unresponsive to Congress on compounding related matters," and that FDA would "create onerous regulations that do little to improve patient

safety while significantly raising costs to patients and impeding the ability of small, community pharmacies to survive."[23]

Efforts to restrict FDA actions against compounders continued as the Obama Administration prepared to take office. In a January 12, 2009, letter to then-President-Elect Obama and Senator Tom Daschle, a key HHS transition official, IACP wrote:

> misguided efforts by the FDA to alter the regulatory landscape threaten pharmacists ability to practice compounding.... IACP is fighting in courts, in Congress and in the public arena to ... maintain states' historically established authority over the practice of pharmacy compounding.[24]

In a draft "Stakeholder Meeting Template" form filled out by IACP during the transition, the organization suggested that President Obama issue "a possible Executive Order to remedy the FDA's expansive overreach" and support a change to FDA law to "clarify that compounded preparations are not subject to the FDA approval process and manufacturing requirements."[25] The Obama Administration did not issue such an order.

In 2010, IACP drafted legislation to "provide pharmacists with an explicit exemption from FDA approval and FDA manufacturing requirements."[26] At a board meeting, documents indicate that IACP leaders discussed efforts to move this legislation through Congress, including lobbying for Congressional hearings on FDA's lack of authority over compounders.[27] They created a draft release titled "*FDA's Questionable Jurisdiction and Prescription Compounding Need for Senate Oversight Hearings*." In it, IACP stated:

> The International Academy of Compounding Pharmacists (IACP) and the U.S. Food and Drug Administration (FDA) continue to disagree regarding the FDA's jurisdiction to regulate pharmacy compounding of prescription medicines. ... While IACP respects the FDA's proper and legal regulation of pharmaceutical manufacturers, state laws specifically state that State Boards of Pharmacy are

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[23] International Academy of Compounding Pharmacists, *Compounding Legislation: It Hurts Everyone* (Mar. 2007).

[24] Letter from L.D. King, Executive Director, International Academy of Compounding Pharmacists, to President-Elect Barack Obama and the Honorable Tom Daschle (Jan. 12, 2009).

[25] International Academy of Compounding Pharmacists, *Health Policy Stakeholder Meeting Template (draft)* (Jan.7, 2009).

[26] International Academy of Compounding Pharmacists, *Board of Directors Meeting* (2010).

[27] *Id.*

responsible for regulating pharmacy compounding (including veterinary compounding).[28]

The efforts by IACP to restrict FDA authority and limit regulation of compounders to the states raise additional concerns because IACP was at the same time attempting to limit efforts by state regulators to create more stringent compounding standards. In a 2003 update for the IACP Board of Directors, IACP staff described efforts to intervene in Iowa to weaken proposed state labeling requirements, in Arkansas to modify proposed bans on compounding products that are "copies of commercially available FDA-approved drug products," and in Texas to weaken proposed regulations on the use of "bulk active pharmaceutical ingredients (APIs) to compound for animals."[29]

In an undated internal communication, IACP staff expressed concerns that "FDA has engaged in informal conversations with several State Boards of Pharmacy, encouraging state agencies to add restrictions to pharmacy laws and regulations applicable to veterinary compounding."[30] One IACP strategy was to ensure that more compounders served as members of state boards of pharmacy. In a 2005 public affairs memo to the IACP's Executive Director, officials wrote of the need to "develop [a] state Boards of Pharmacy strategy."[31] They wrote that "a larger goal for the profession is garnering more awareness and representation with individual state Boards of Pharmacy. Although there have been efforts to place compounding pharmacists on board, we believe a comprehensive plan makes sense. A few places to begin include: … Secure representation of compounding pharmacies on Boards…[and] identify and educate potential allies on existing state boards."[32]

IACP Guidance on Circumventing FDA Inspection Authority

Documents obtained by the Committee reveal that IACP staff disseminated guidance documents to pharmacists that recommended ways pharmacists could obstruct FDA oversight of their facilities. Two of the guidance documents were titled "Knowing your legal rights and

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[28] International Academy of Compounding Pharmacists, *FDA's Questionable Jurisdiction and Prescription Compounding Need for Senate Oversight Hearings* (undated).

[29] International Academy of Compounding Pharmacists, *IACP Board of Directors Meeting: State Update* (Oct. 22, 2003).

[30] International Academy of Compounding Pharmacists, *Compounding for Animals Issue Briefing*.

[31] Memorandum from Bob Chlopak, Josh Wonderoff, Tammy Gordon, Chlopak, Leonard, Schecter, and Associates, to L.D. King and Jennifer Goodrum, International Academy of Compounding Pharmacists (Aug. 9, 2005).

[32] *Id.*

having a clear policy in place will help you respond effectively when FDA inspects your pharmacy" and "FDA Warning Letters to Compounding Pharmacies: What They Are, What They Say, and What to Do If You Get One."[33] IACP described these documents as a way to help pharmacists "deal with the big, bad FDA."[34]

In drafting guidance materials for pharmacists, IACP representatives instructed their outside consultant to "be specific and expand upon what the Constitutional rights of the pharmacy/pharmacist are and what they are obligated to do; not obligated to do and what they should NOT do."[35] They further told the consultant that "there should be guidance on when to contact one's attorney and when it is appropriate to end the visit by the FDA and when lines have been overstepped."[36] The documents drafted for IACP included numerous ways for pharmacists to restrict FDA access to their facilities and to question the agency's authority. They included the following suggestions:

- "If a pharmacy does not compound, or compounds medication only in the normal course of pharmacy practice and meets the other criteria, FDA's broad inspectional powers to inspect do not apply....Relying on your status as a licenses pharmacy, you could elect to decline the [FDA] investigator's request to see 'manufacturing' records."[37]
- "If you decide to let the investigator have access to some records, never let the investigator rummage through files or records, or roam through the pharmacy unescorted."[38]
- "FDA cannot compel you to answer questions, but any questions that are answered must be answered truthfully. Oral responses may be admissible evidence in any subsequent court actions. If you are in doubt about an answer, you should politely decline to respond at that time by saying, 'Let me check into that.'"[39]
- "Under no circumstances should you give them a formula, invoice or any other piece of paper. Ask specifically if this is a formal FDA investigation. They will reply that it is

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[33] International Academy of Compounding Pharmacists, *FDA Inspections of Pharmacies: What Should You Do?* (undated).

[34] E-mail from Sarah Dodge, International Academy of Compounding Pharmacists, to L.D. King, International Academy of Compounding Pharmacists (Dec. 29, 2008).

[35] E-mail from Dana Reed-Kane, International Academy of Compounding Pharmacists Board of Directors, to Matthew T. Slimp et al. (Feb. 6, 2009).

[36] *Id.*

[37] International Academy of Compounding Pharmacists, *FDA Inspections of Pharmacies: What Should You Do?* (undated).

[38] *Id.*

[39] *Id.*

> not. Regardless of the answer, tell them you are claiming your exemption as a compliant, licensed pharmacy… Be prepared, they probably won't know what to do if you refuse to give out paperwork."[40]

Other guidance documents show that IACP also provided guidance on how to restrict FDA from taking samples from compounders. When FDA sought to collect samples as part of a 2005 formal study, IACP stated "Unauthorized FDA inspections create uncertainty and harm pharmacies and the patients they serve."[41] In October 2008, an IACP representative alerted members in Ohio about possible FDA inspections relating to estriol, stating, "It is advised that pharmacies not sign any FDA documents."[42]

In 2009, IACP hired an outside consultant to develop a seminar "to focus on the balancing of what you need to do when the FDA comes knocking on your door to be compliant and what you DON'T need to do (and shouldn't do) to protect your Constitutional rights."[43] Specifically, IACP's representative requested "some really strong messaging inserted into the presentation about … when a pharmacist should NOT provide certain information to the FDA."[44] IACP also wanted to "note likely situations when the FDA is overstepping its bounds and when pharmacists should draw the line and discontinue the visit and call their attorney."[45] IACP described the seminar as a way "to prevent pharmacists from potentially self-incriminating or giving the FDA information that could put pharmacists in a position to be sued by patients or others."[46]

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[40] International Academy of Compounding Pharmacists, *What should you do if a representative from the Food and Drug Administration (FDA) requests a sample of your Active Pharmaceutical Ingredient (API)?* (undated).

[41] International Academy of Compounding Pharmacists, *FDA Sampling of Compounded Medications* (undated).

[42] E-mail from International Academy of Compounding Pharmacists, to Sarah Dodge, International Academy of Compounding Pharmacists (Oct. 27, 2008).

[43] E-mail from Sarah Dodge, International Academy of Compounding Pharmacists, to Dana Reed-Kane, International Academy of Compounding Pharmacists Board of Directors (Feb. 5, 2009).

[44] *Id.*

[45] *Id.*

[46] *Id.*

IACP's Legal Advice on FDA's Regulatory and Enforcement Authority

IACP also injected itself into administrative proceedings when individual pharmacies were accused of causing adverse events. In doing so, the organization consistently focused on questions regarding FDA authority. In 2003, "a large pharmacy in California" received a letter from FDA accusing them of acting as a manufacturer.[47] In internal communications, IACP representatives expressed concerns about the "the volume and scope of this pharmacy may be distributing," but noted that "the precedence of FDA using volume, and commercial scale equipment to deem a pharmacy a manufacturer warrants a response from us."[48] Ultimately, documents reveal that the pharmacy "paid [IACP's] attorney to write a response on behalf of IACP."[49]

In 2005, Triangle Compounding Pharmacy faced possible disciplinary action in North Carolina because a patient had died of a lidocaine overdose from one of its products. Board minutes from 2006 show that IACP responded to the North Carolina Board of Pharmacy's proceedings with a letter in which they "cautioned ... against relying on certain factors when considering possible disciplinary action against Triangle Compounding Pharmacy."[50]

In 2006, in response to an FDA letter expressing concern that a pharmacy called Pharmacy Creations was acting as a manufacturer, IACP appears to have provided the pharmacy with specific guidance on the "attack" the pharmacy should make in response to FDA's warning letter, which included challenging FDA's ability to enforce its guidance against the pharmacy.[51] A senior IACP representative wrote that FDA compounding "CPGs are unenforceable and flawed."[52]

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[47] E-mail from L.D. King, International Academy of Compounding Pharmacists, to Mike Leake et al. (Jan. 16, 2003).

[48] *Id.*

[49] *Id.*

[50] International Academy of Compounding Pharmacists, *Government and Regulatory Affairs – Consent Agenda Items* (Oct. 11, 2006).

[51] Letter from Frank P. Arleo, Arleo & Donohue, LLC, to Maryann Muncon, Office of Compliance, Centers for Drug Evaluation & Research, Food and Drug Administration (Dec. 28, 2007).

[52] E-mail from L.D. King, International Academy of Compounding Pharmacists, to Scott (Nov. 6, 2006).

Conclusion

The documents the Committee has received reveal that for almost two decades, IACP has fought to restrict FDA authority over drug compounders, even when top organization officials recognized public health concerns with compounding practices. These efforts succeeded in creating considerable uncertainty about FDA's regulatory authority. As we seek to understand why the regulatory system failed in protecting patients from the unsafe drugs produced by NECC, this is a key part of the story.

For this reason, we believe that Mr. David Miller, Executive Vice President and CEO of IACP, should be invited to testify at the April 16 pharmacy compounding hearing.

Sincerely,

Henry A. Waxman
Ranking Member

Diana DeGette
Ranking Member
Subcommittee on Oversight
and Investigations

John D. Dingell
Member

Edward J. Markey
Member

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

The Honorable Tim Murphy
Chairman
Subcommittee on Oversight and Investigations
Committee on Energy and Commerce
House of Representatives
Washington, D.C. 20515-6115

JUL 11 2013

Dear Mr. Chairman:

Thank you for providing the opportunity for the Food and Drug Administration (FDA or the Agency) to testify at the April 16, 2013, hearing before the Subcommittee on Oversight and Investigations entitled "A Continuing Investigation into the Fungal Meningitis Outbreak and Whether It Could Have Been Prevented." We provided a partial response to questions posed by certain Members of the Committee on May 22, 2013. This is our final response, incorporating responses to questions posed by Representatives Bill Johnson and Renee Ellmers.

If you have further questions, please let us know.

Sincerely,

Karen Mestel
for

Michele Mital
Acting Associate Commissioner
for Legislation

We have restated each Member's questions below in bold, followed by FDA's responses.

The Honorable Tim Murphy

1. **Please explain the new policy and process FDA has established to enhance communications with the State pharmacy boards.**

   Working with our state and local partners is a priority. We have been coordinating with the states during our inspections of pharmacies that may pose higher risks and are known to have produced sterile drug products in the past, and we are providing updated information regarding our inspections to appropriate regulators. FDA coordinated our inspections with state officials, who have accompanied our investigators in most cases, including 28 of 31 (90 percent) of the priority inspections, and all of the 26 for-cause inspections. Moreover, inspection observations on FDA Form 483s[1] and Warning Letters are being posted on our website for states and the public to see. This is important because many of these facilities ship across state lines.

   In addition, we have conducted training for some states and are working on a plan for additional interactions, regardless of whether we do or do not get Federal legislation. We have had conversations with five state Boards of Pharmacy, attended the National Governors Association policy committee meeting, and held at least bi-weekly calls with the National Association of Boards of Pharmacy, and we intend to continue these state outreach efforts to improve our communications with states. We are also exploring other ways to provide useful information to state regulators.

2. **Please explain what steps have been taken to ensure that Warning Letters and related correspondence are approved in a timelier manner.**

   Warning Letters are an important regulatory tool and serve as the Agency's principal means of achieving prompt voluntary compliance with the Federal Food, Drug, and Cosmetic Act (FD&C Act). FDA issues Warning Letters to address violations of regulatory significance and may follow with an enforcement action if the violations are not promptly and adequately corrected.

   FDA takes very seriously the importance of approving and issuing Warning Letters and related correspondence in a timely manner, and we are taking steps to increase our timeliness and efficiency. For example, FDA is conducting a "Lean Project Improvement Initiative," aimed in part at improving the efficiency with which the Agency issues Warning Letters involving human drug products by identifying areas

[1] An FDA Form 483 is issued when investigators observe any significant objectionable conditions. It does not constitute a final Agency determination of whether any condition is in violation of the FD&C Act or any of our relevant regulations but the observations often serve as evidence of a violation of the FD&C Act and its implementing regulations.

for process improvement and working to standardize the process. This would include Warning Letters related to compounding.

In addition, with respect to pharmacy compounding, in several instances in the past, the issuance of Warning Letters and subsequent correspondence has been delayed by pharmacies' challenges to FDA's authority, court decisions, and other complexities and ambiguities in the law. Legislation that provides FDA with appropriate authority over firms that produce and ship interstate sterile drugs in advance of or without a prescription would help the Agency to issue Warning Letters and related correspondence and take appropriate enforcement action more efficiently.

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?**

In the context of compounding pharmacy inspections, FDA typically considers conducting a "for cause" inspection in response to a report of a serious adverse event that is associated with a product quality issue or practice that may have caused the drug to be adulterated or misbranded. FDA may also consider conducting a for-cause inspection in response to a request from a State Board of Pharmacy.

FDA conducts "proactive" inspections when routine surveillance is appropriate in the absence of a specific reason to inspect.

We are not aware of the decision to suspend routine, proactive inspections of compounding pharmacies as having been made by any one individual.

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?**

FDA's proposed framework would make a distinction between two categories of compounding: traditional and non-traditional. Traditional compounding would include the combining, mixing, or altering of ingredients to create a customized medication for an individual patient with an individualized medical need for the compounded product, in response to a valid patient-specific prescription or order from a licensed practitioner documenting such medical need. Under our proposal,

hospital pharmacies would be classified as traditional compounding pharmacies. Traditional compounding, while posing some risk, plays an important role in the health care system, and should remain the subject of state regulation of the practice of pharmacy. Health systems are entrusted with and liable for the care of their patients, and their compounding pharmacy activities are just one aspect of that care. That responsibility for patient care creates incentives that do not exist in the same way for pharmacies outside of hospital systems.

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?

The fungal meningitis outbreak has caused us to re-examine our past practices with regard to our oversight of compounding pharmacies, and in coordination with state officials, FDA recently conducted its own risk-based inspections of sterile practices at certain compounding pharmacies that may pose higher risks and are known to have produced sterile drug products in the past. The objective of these inspections was to determine whether these compounding pharmacies posed a significant threat to public health from poor sterile processing practices.

To ensure a consistent approach, the Agency inspected against the current Good Manufacturing Practice (cGMP) standards. This avoided the use of different standards for pharmacies based on differences in state law or the application of the FD&C Act. In addition, the Agency has considerable experience with its cGMPs, a national standard that helps ensure the production of quality, safe, sterile drug products.

The decision to focus on Federal standards for sterile practices provides a consistent approach to reviewing the quality of sterile drug products made at different firms across the country. When we observed conditions that may constitute violations of the FD&C Act during any of the inspections, at the close of the inspection, we issued an FDA Form 483, listing our inspection observations. Whether FDA will take action based on these standards will depend upon the facts of each specific case. If a compounded drug product does not meet the exemptions under section 503A of the FD&C Act (to the extent they are applicable) or the conditions for exercise of enforcement discretion under FDA's Compounding Compliance Policy Guide, FDA could issue a Warning Letter or take enforcement action such as a seizure or injunction. If, based on information reviewed during the inspection and discussion with the firm, the firm's drug production activities appear more like those within the bounds of traditional pharmacy practice and not conventional manufacturing, FDA intends to refer the matter to the state that licensed the pharmacy for further action, noting the sterile processing deficiencies we observed.

Are you partnering with and in discussions with State Board of Pharmacies to determine if the pharmacy has exceeded state licensing authorities?

FDA is working closely with the states and will be providing updated information regarding our inspections to appropriate regulators. Inspection observations on FDA Form 483s and Warning Letters are being posted on our website for states and the public to see. This is important because many of these facilities ship across states. In addition, FDA coordinated our proactive inspections with state officials, who have accompanied our inspectors in almost all cases.

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?**

   Unlike conventional drug manufacturers, by law, compounding pharmacies are not required to register with FDA if they meet certain conditions. Pursuant to section 510(g) of the FD&C Act, pharmacies are exempt from registration if they comply with applicable local laws regulating the practice of pharmacy and medicine, regularly engage in dispensing drugs upon a prescription from a licensed practitioner, and do not manufacture, prepare or compound drugs for sale other than during the regular course of their business of dispensing or selling drugs at retail.

   A pharmacy's voluntary registration may provide FDA with information about the facility, such as its name, location, and ownership structure, but voluntary registration alone does not give FDA additional authority over the pharmacy. In fact, a compounding pharmacy might register with FDA to give the impression that the Agency provides a higher level of oversight or approval of the pharmacy's activities than it actually does.

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?**

   If an establishment refuses to allow FDA investigators to enter or permits the investigators to enter but refuses to permit access to information that the Agency needs, and believes it has authority, to review, the Agency can seek an administrative warrant. In some circumstances, FDA seeks an administrative warrant before attempting an inspection, if it has reason to believe that the firm will refuse an inspection.

Generally speaking, the process for obtaining a warrant involves the following steps: (1) the relevant FDA District Office recommends that a warrant be obtained and prepares a recommendation that describes the refusals investigators have encountered and the information sought; (2) the District Office's draft application is reviewed concurrently by the Division of Enforcement within the Office of Regulatory Affairs' Office of Enforcement and Import Operations and the relevant Center (e.g., the Office of Compliance in the Center for Drug Evaluation and Research for warrants related to compounding pharmacies); (3) the Agency's Office of the Chief Counsel reviews the draft warrant and application for legal sufficiency, and then provides the papers to the Division of Enforcement to transmit to the Department of Justice's (DOJ) Consumer Protection Branch for review; (4) following review by DOJ's Consumer Protection Branch, the local United States Attorney's Office receives the papers and assigns an Assistant United States Attorney, who then arranges a meeting with the investigator and a Magistrate Judge to get the warrant signed by the Magistrate Judge; (5) after the warrant is signed, arrangements are made in most cases for the U.S. Marshal's Service to accompany the investigators as they attempt to execute the warrant.

Over the past five years, FDA has sought and obtained about six administrative warrants for compounding pharmacies. This figure does not include situations where the Agency was able to resolve a refusal by some other means (e.g., a conversation between FDA's Office of Chief Counsel and the firm's attorney). We have not identified a situation where a Judge refused to sign an administrative warrant sought by FDA, but we note that our records on administrative warrants are somewhat limited. Also, our records are not kept in a way that would enable us to readily calculate the average the length of time it takes for FDA to obtain an administrative warrant, and the length of time can depend on a variety of factors. We estimate that the average time to obtain a warrant is two weeks. In the most recent administrative warrant we sought for a pharmacy, 10 days passed between when the refusal was encountered and when the warrant was signed by the Magistrate Judge.

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.**

While FDA is unable to comment specifically regarding NECC or Ameridose due to the ongoing investigations, we have listed below reports of adverse events associated with NECC and Ameridose products that FDA identified based on a search of readily available records, including the FDA Adverse Event Reporting System (FAERS) database. Thus, this listing of reports may not be an all-inclusive list. For each identified report, the list indicates whether FDA is able to confirm having communicated information about the report to the Massachusetts Board of Registration in Pharmacy (MA Board of Pharmacy).

NECC

A comprehensive search of the FDA Adverse Event Reporting System (FAERS) database identified 52 reports associated with NECC between 2002 and September 26, 2012. The MA Board of Pharmacy was notified about five of the 52 reports by FDA. Thirty-nine of the reports were related to a single product, and FDA's investigation did not identify evidence of a product quality deficiency. Two reports were isolated adverse events, and six reports did not raise a signal for product quality issues. These reports include:

- In March 2002, FDA received two reports describing dizziness, shortness of breath, diaphoresis, and drop in blood pressure following administration of betamethasone injection. The MA Board of Pharmacy was notified, and FDA and the MA Board of Pharmacy conducted simultaneous, but independent, investigations in April 2002. FDA investigators were unable to complete the investigation because NECC management contested FDA's authority to inspect and refused to provide necessary records.

- In July and August 2002, FDA received three MedWatch reports describing two cases (two of the reports described the same case) of meningitis in patients who received injections of methylprednisolone acetate prepared by NECC. The MA Board of Pharmacy was notified; FDA and the MA Board of Pharmacy conducted a joint inspection, and an FDA-483[2] list of inspectional observations was issued in February 2003. FDA lab analysis identified bacterial contamination. Based upon the evidence available to them, FDA and the MA Board of Pharmacy jointly determined that NECC at that time was operating as a compounding pharmacy and, therefore, the state would be in a better position to obtain compliance or take regulatory action as necessary. NECC recalled 15 lots of methylprednisolone acetate that were labeled with an incorrect expiration date; this included the lot that was found to be contaminated.

- In 2007, FDA received six reports associated with Avastin repackaged by NECC for patients enrolled in a Visudyne Registry Study of Age-Related Macular Degeneration (AMD) Therapy. Reports were submitted in accordance with the Visudyne Registry Study protocol. Four patients aged 77 or older died. The cause of death was reported as unknown. Product quality complaints for NECC's repackaged Avastin were not reported, and these reports do not raise a signal for product quality issues. The MA Board of Pharmacy was not notified by FDA.

- FDA received a report in June 2007 describing a case of endophthalmitis in a patient who received an injection of Avastin repackaged by NECC. This was an

[2] An FDA Form 483 is issued when investigators observe any significant objectionable conditions. It does not constitute a final Agency determination of whether any condition is in violation of the FD&C Act or any of our relevant regulations, but the observations often serve as evidence of a violation of the FD&C Act and its implementing regulations.

individual adverse event. For such isolated reports, it is rarely possible to know with a high level of certainty whether the event was caused by the product. The MA Board of Pharmacy was not notified by FDA.

- In December 2007, FDA received 39 reports that appeared to have been filled out by individual patients but all were submitted together in one batch. The reports described flu-like symptoms in fibromyalgia patients treated with betamethasone compounded by NECC, which the patients' physician attributed to lack of efficacy. FDA conducted an investigation at the office of the patients' physician and collected samples of betamethasone. FDA did not find any information to suggest that the adverse events were caused by deficiencies in the quality of the betamethasone made by NECC, and FDA laboratory analysis indicated that the samples met specifications for endotoxins, assay, and identification. The MA Board of Pharmacy was not notified by FDA.

- FDA received a report in September 2009 describing endophthalmitis in a patient who received an injection of Avastin repackaged by NECC. This was an individual adverse event. For such isolated reports, it is rarely possible to know with a high level of certainty whether the event was caused by the product. In addition, the report indicated that approximately 40-50 other patients had received Avastin from the same lot that was associated with this event, and that no other adverse events were reported. The MA Board of Pharmacy was not notified by FDA.

FDA also received an October 2008 report of an adverse event through its Consumer Complaints database. This report describes a patient who was treated for a bacterial infection and other symptoms after chelation therapy with phosphatidylcholine, prepared by NECC. FDA collected a sample, and laboratory analysis indicated that the product failed to meet label claims for potency, but tested negative for microbial contamination. A recall was not pursued because there was no evidence of contamination and the product lot had expired when the sample results were received. The MA Board of Pharmacy was not notified by FDA.

Ameridose

FDA's search of FAERS for reports related to Ameridose identified 18 reports. Eleven of the reports describe adverse events and are listed below. Three of these reports (including two reports received from different sources describing the same incident) describe adverse events in patients receiving several drug products prepared by various firms, and Ameridose's product was not considered suspect. Three reports do not describe adverse events that are considered serious or unexpected, and five reports describe possible lack of efficacy of drug products made by Ameridose. None of these reports suggested sterility concerns. The MA Board of Pharmacy was not notified about these reports by FDA.

- In April 2008, FDA received a report indicating that succinylcholine supplied in prefilled syringes had an unpredictable clinical effect, at times producing inadequate or no muscle relaxation.

- FDA received a report in November 2008 describing intermittent lack of effect from phenylephrine syringes. The reporter indicated that several syringes were returned to the vendor, which reported back that the syringes were "fine."

- In March and June 2010, FDA received two reports from different manufacturers describing the same incident, in which a patient's arm turned white and needed to be amputated after several drugs, including midazolam, made by Ameridose, were infused into an artery instead of a vein. The reporter indicated that the adverse events were related to administration of a drug made by a different manufacturer.

- In June 2011, FDA received a report regarding a patient who was administered products, including a promethazine HCl and sodium chloride bag made by Ameridose, and Reglan, made by a different firm. She experienced decreased respirations, decreased blood pressure, and unresponsiveness after administration of Reglan (not supplied by Ameridose), which was considered suspect. The reporter considered the adverse events to be related to the combination of promethazine and Reglan.

- FDA received a report in November 2011 describing three patients who reported poor pain control from a ropivacaine + fentanyl epidural injection. The reporter indicated that Ameridose had been contacted.

- FDA received a report in March 2012 regarding a patient who was not adequately sedated with a dose of midazolam 1mg/mL and required an additional 4mg to achieve sedation. The report noted that Ameridose was contacted about the potential problem and was conducting an investigation.

- In July 2012, FDA received a report describing lack of muscle relaxation in a patient who received succinylcholine chloride made by Ameridose. The reporter suspected that the drug was not refrigerated properly and degraded.

- In September 2012, FDA received three reports from the same reporter describing "post-operative agitation and excitation" in patients who received methohexital during electroconvulsive treatment. The reports indicated that potency results and all other testing were within specification. Also, side effects such as restlessness and anxiety are included in the approved product labeling.

2. Please describe how Adverse Event Reports submitted to FDA's MedWatch system are shared with the correct FDA offices and employees.

FDA implemented the MedWatch program to learn of adverse experiences that patients have encountered. FDA requires manufacturers to report adverse experiences to FDA and encourages voluntary reports from consumers and health professionals. FDA also accepts reports submitted electronically at *www.fda.gov/medwatch/report.htm*. FDA uses these MedWatch reports to identify problems in marketed products.

Voluntary reports are essential for ensuring the continued safety of FDA-regulated products. Reports submitted to MedWatch are added to existing data in our Adverse Event Reporting System database and reviewed by FDA's post-marketing safety staff for the appropriate product areas. The collected reports are monitored and observed for emerging patterns. One or two well-documented case reports may provide an early signal of unexpected safety issues and lead to additional evaluation. This may result in FDA actions that improve the safety of the products used in patient care each day. We carefully evaluate and analyze all reports that are available to us and make recommendations for possible actions, if the science-based risk evaluation warrants the actions.

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?**

Although we cannot comment on Ameridose specifically due to the ongoing FDA investigation, in the context of compounding pharmacy inspections, FDA typically considers conducting a "for cause" inspection in response to a report of a serious adverse event that is associated with a product quality issue or practice that may have caused the drug to be adulterated or misbranded. FDA may also consider conducting a for-cause inspection in response to a request from a State Board of Pharmacy.

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.**

FDA searched its readily available records for complaints related to NECC and Ameridose that the Agency received between 2002 and September 25, 2012, and did not identify any complaints that FDA is able to confirm having forwarded or reported to the Massachusetts Board of Pharmacy. However, some complaints were sent to both FDA and the Massachusetts Board of Registration in Pharmacy, and some were investigated jointly.

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 pharmacy.[3] 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 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 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 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.**

In response to Questions 1, 2, and 3, we note that of compounded products, sterile compounded products made in advance of or without a prescription and shipped interstate pose the highest risks to the most people if they are not made in accordance with strict quality standards. FDA is proposing to define non-traditional compounding based on factors that make the product higher risk, such as any sterile compounding in advance of or without receiving a prescription, where the drug is distributed out of the state in which it was produced. Under this proposal, FDA would hold these compounders to Federal quality standards adequate to ensure that the compounding could be performed without putting patients at undue risk; conduct proactive inspections; ensure that the firms comply with required adverse event reporting and labeling; and take appropriate enforcement action when necessary to protect the public health.

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[3] *http://markey.house.gov/press-release/markey-report-compounding-pharmacies-going-untracked-unregulated-under-inspected-coast#overlay-context*

Likewise, the states must assume more responsibility in monitoring the compounding of sterile products that are made in response to patient-specific prescriptions and those that are distributed only in a single state, as well as the compounding of non-sterile products. States have a variety of different laws and regulations and varying levels of resources and expertise to oversee compounding pharmacies. They apply different standards and enforce them differently. At the 50-state meeting, we heard from states that while they feel comfortable regulating pharmacies that operate within their states, they have concerns about pharmacies located out of their state that ship into the state and that may not be tightly regulated, placing their citizens at risk. FDA's proposal to regulate interstate shipment of the highest-risk, sterile-compounded products should alleviate some of these concerns.

FDA is willing to assist the states in developing and implementing appropriate product quality standards. FDA already has conducted training for some states and is working on a plan for additional interactions with the states, regardless of whether new Federal legislation is or is not enacted.

4. **The report indicated that states do not have the 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 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 FDA support the requirement that compounding pharmacies provide information on the volume of drugs to FDA or the states?**

   A requirement for firms engaging in non-traditional compounding; i.e., those that produce and distribute interstate sterile products in advance of or without a prescription—to report information regarding the volume of drugs they compound to the Agency would be helpful. In addition, states could consider whether a state requirement for pharmacies engaging in traditional compounding to report such information to the states may assist states' regulation of these entities. Reporting the volume of compounded drugs to FDA or the states would help regulators to identify those pharmacies that are the largest producers of compounded drugs and help to prioritize inspection and surveillance resources.

   b. **Would FDA find it helpful to have this information, for purposes of determining which of these facilities may be manufacturing drugs and are all therefore subject to the requirements of drug manufacturers?**

   Information regarding volume would be helpful; it would provide data on high-producing pharmacies so that the Agency could prioritize inspections and use its resources to best protect the public health. For example, FDA is particularly concerned about the large-scale distribution of compounded sterile drug products to

health care facilities nationwide, when compliance with appropriate standards for large-scale production has not been met.

However, determining whether a firm is acting as a manufacturer or a pharmacy compounder is very fact-specific. Sometimes a state-licensed pharmacy may be simultaneously engaging in some activities that are considered traditional compounding while other activities are more like typical manufacturing, further complicating the determination of the facility's regulatory status. Therefore, while volume information is helpful, it is critical that FDA have clear authority to examine pharmacy records.

For all compounders, traditional and non-traditional, FDA should have clear authority to examine records, such as records of prescriptions received, products shipped, volume of operations, and operational records such as batch records, product quality test results, and stability testing results. Such inspections are necessary to determine when a pharmacy exceeds the bounds of traditional compounding, to facilitate FDA's response to public health threats, and to enforce Federal standards when appropriate.

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 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 these states to identify issues pertaining to safety, cleanliness, sterility and other issues that came to light in the NECC 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?**

As noted above, FDA is proposing to define non-traditional compounding based on factors that make the product higher risk such as any sterile compounding in advance of or without receiving a prescription, where the drug is distributed out of the state in which it was produced.

Likewise, the states must assume more responsibility in monitoring the compounding of sterile products that are made in response to patient-specific prescriptions and those that are distributed only in a single state, as well as the compounding of non-sterile products. States have a variety of different laws and regulations and varying levels of resources and expertise to oversee compounding pharmacies. They apply different standards and enforce them differently. At the 50-state meeting, we heard from states that while they feel comfortable regulating pharmacies that operate within their states, they have concerns about pharmacies located out of their state that ship into the state and that may not be tightly regulated, placing their citizens at risk.

FDA's proposal to regulate interstate shipment of the highest-risk, sterile-compounded products should alleviate some of these concerns. Likewise, the states must assume more responsibility in monitoring the compounding of all products that are marked intrastate.

The Honorable G.K. Butterfield

1. **Will sequestration impact 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?**

   Sequestration will reduce FDA funding, which will have a variety of adverse impacts on FDA's programs, including the Agency's ability to inspect compounding facilities, and address complaints associated with compounded drugs to the extent we could with more funds.

2. **Does reassigning investigators who would normally be conducting inspections at conventional drug manufacturers divert resources from other areas including pharmaceutical approval?**

   Yes, the funding to conduct the 31 proactive inspections, as well as the 26 recent for-cause inspections comes out of existing funding for drug manufacturing inspections—including pre-approval inspections—and pulls from the same inspection force. The number of investigators who have the training to conduct these inspections is limited, and the investigators conducting the compounding inspections also conduct pre-approval and other types of inspections. The current staffing of compounding inspections is not sustainable in the longer term, without harming our ability to oversee the 5,600 conventional manufacturers we regulate. It is also important to note that the proactive inspections FDA has conducted are a fraction of the compounding pharmacy industry. As we have previously said, we do not know how many pharmacies there are since they do not register; however, according to the International Academy of Compounding Pharmacists, an estimated 28,000 pharmacies do some degree of compounding. Even with a limited group of 500-1000 non-traditional compounding pharmacies over which FDA has proposed that it would have proactive authorities, at current funding levels, FDA projects that it would inspect each pharmacy only once every 25-50 years.

3. **In the risk-based framework recommended by FDA, would the Agency have the appropriate resources to test samples of compounded drugs and examine records of compounding pharmacies?**

   As Dr. Hamburg noted in her testimony, we look forward to working with Congress to explore the appropriate funding mechanisms to support this work, which could include registration or other fees, as Congress has authorized and FDA has successfully implemented in other settings. Providing establishment and reinspection

fees to help defray the cost of enhanced oversight would significantly improve the current oversight of compounders.

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 FDA? What standards are enforced on these registered pharmacies?**

Unlike conventional drug manufacturers, by law, compounding pharmacies are not required to register with FDA if they meet certain conditions. Pursuant to section 510(g) of the FD&C Act, pharmacies are exempt from registration if they comply with applicable local laws regulating the practice of pharmacy and medicine, regularly engage in dispensing drugs upon receiving a prescription from a licensed practitioner, and do not manufacture, prepare or compound drugs for sale other than during the regular course of their business of dispensing or selling drugs at retail.

A pharmacy's voluntary registration may provide FDA with information about the facility, such as its name, location, and ownership structure, but voluntary registration alone does not give FDA additional authority over the pharmacy. In fact, a compounding pharmacy might register with FDA to give the impression that the agency provides a higher level of oversight or approval of the pharmacy's activities than it actually does.

5. **What improvements in communication and oversight have been implemented by FDA in response to meetings with State Pharmacy boards?**

Working with our state and local partners is a priority. We have been coordinating with the states during our inspections of pharmacies that may pose higher risks and are known to have produced sterile drug products in the past, and we are providing updated information regarding our inspections to appropriate regulators. FDA coordinated our inspections with state officials, who have accompanied our investigators in most cases, including 28 of 31 (90 percent) of the priority inspections, and all of the 26 for-cause inspections. Moreover, inspection observations on FDA Form 483s and Warning Letters are being posted on our website for states and the public to see. This is important because many of these facilities ship across state lines.

In addition, we have conducted training for some states and are working on a plan for additional interactions, regardless of whether or not new Federal legislation is enacted. We have had conversations with five state Boards of Pharmacy, attended the National Governors Association policy committee meeting, and held at least bi-weekly calls with the National Association of Boards of Pharmacy, and we intend to continue these state outreach efforts to improve our communications with states. We are also exploring other ways to provide useful information to state regulators.

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?

It is important to note that a drug recall is a voluntary action; FDA does not have mandatory drug recall authority. Firms that produce drug products, including compounded drugs, may decide to recall products that are defective or potentially harmful. In such cases, as part of the recall, the firm would notify those who have received the product, including consumers and health care professionals. When the Agency is advised of a firm's intent to recall, FDA's role is to monitor the company's strategy, including its communication strategy, and to assess the adequacy of the recall.

FDA works with industry and our Federal and state partners to issue public notices about recalls of drug products that may present a significant or serious risk to the consumer or user of the product. Not all recalls rise to the level of issuing press releases. FDA seeks publicity when the recalling firm does not adequately alert the public to recalls of products that pose a serious hazard. In such cases, FDA can hold press conferences, issue press releases, and post updates to its website.

FDA posts information pertaining to recalls on its website. For example, FDA's weekly "Enforcement Report" (*http://www.fda.gov/Safety/Recalls/EnforcementReports/default.htm*) lists all recalls overseen by FDA, including those that have been classified by FDA and those that are pending classification (these are reposted with their classification in the Enforcement Report once that determination has been made). FDA also has a "major recalls" webpage (*http://www.fda.gov/Safety/Recalls/MajorProductRecalls/default.htm*), which includes details of FDAs involvement in investigating recalls, a means to search recalled products, and information for consumers and industry representatives.

FDA's MedWatch program may also publish drug safety alerts that provide timely new safety information on FDA-regulated products and contain actionable information that may affect both treatment and diagnostic choices for healthcare professionals and patients. When indicated, FDA also publishes drug safety communications in both English and Spanish on its website to provide the public with access to important drug safety information. The webpage contains the most recent Drug Safety Communications (which may include advice to healthcare providers and patients as well as questions and answers) and links to pertinent safety information, such as Early Communications, Follow-Up Early Communications, Information for Healthcare Professional sheets, and Public Health Advisories. (*http://www.fda.gov/Drugs/DrugSafety/ucm199082.htm*).

In addition, FDA Drug Safety Podcasts are produced by FDA's Center for Drug Evaluation and Research (CDER). They provide emerging safety information about

drugs in conjunction with the release of Public Health Advisories and other drug safety issues.

Many of these communications are further disseminated through electronic distribution lists and through Twitter and Facebook.

7. **What additional legal framework would provide FDA with the tools needed to identify and adequately regulate pharmacies to prevent product contamination?**

Recognizing the history of compounding practice, FDA supports the long-standing policy that all compounding should be performed in a licensed pharmacy by a licensed pharmacist (or a licensed physician), and that there must be a medical need for the compounded drug.

Further, there should be a distinction between two categories of compounding: traditional and non-traditional. Traditional compounding would include the combining, mixing, or altering of ingredients to create a customized medication for an individual patient with an individualized medical need for the compounded product, in response to a valid patient-specific prescription or order from a licensed practitioner documenting such medical need. Traditional compounding, while posing some risk, plays an important role in the health care system, and should remain the subject of state regulation of the practice of pharmacy.

Non-traditional compounding would include certain types of compounding for which there is a medical need but that pose higher risks. FDA proposes working with Congress to define non-traditional compounding based on factors that make the product higher risk such as any sterile compounding in advance of or without receiving a prescription, where the drug is distributed out of the state in which it was produced. Non-traditional compounding would be subject to Federal standards adequate to ensure that the compounding could be performed without putting patients at undue risk, and FDA would inspect against and enforce these Federal standards. Such a definition focuses on the highest risk activities and offers a uniform degree of protection across all 50 states, for highest-risk compounding activities.

Non-traditional compounding should, because of the higher risk presented, be subject to a greater degree of oversight. Sterile products produced in advance of or without a prescription and shipped interstate should be subject to the highest level of controls, established by FDA and appropriate to the activity, similar to cGMP standards applicable to conventional drug manufacturers.

In addition, with noted exceptions, certain products are not appropriate for compounding under any circumstances. These products would include: 1) what are essentially copies of FDA-approved drugs, absent a shortage justification based on the drug appearing on FDA's shortage list; and 2) complex dosage forms such as extended-release products; transdermal patches; liposomal products; most biologics; and other products as designated by FDA. Producing complex dosage forms would

require an approved application and compliance with GMP standards, along with other requirements applicable to drug products made by conventional manufacturers.

There are other authorities that would be important to support this new regulatory paradigm. For example, FDA should have clear ability to collect and test samples of compounded drugs and to examine and collect records in a compounding pharmacy, just as the Agency does when inspecting other manufacturers. FDA should also have clear authority to examine records, such as records of prescriptions received, products shipped, volume of operations, and operational records such as batch records, product quality test results, and stability testing results. Such inspections are necessary to determine when a pharmacy exceeds the bounds of traditional compounding to respond to public health threats and to enforce Federal standards.

An accurate inventory of pharmacies engaged in non-traditional compounding would facilitate appropriate oversight and coordination with state regulators. In addition, FDA looks forward to working with Congress on potential improvements that may include label statements and adverse event reporting that have proven useful in other areas.

The Honorable Peter Welch

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

   Unlike conventional drug manufacturers, by law, compounding pharmacies are not required to register with FDA if they meet certain conditions. Pursuant to section 510(g) of the FD&C Act, pharmacies are exempt from registration if they comply with applicable local laws regulating the practice of pharmacy and medicine, regularly engage in dispensing drugs upon a prescription from a licensed practitioner, and do not manufacture, prepare or compound drugs for sale other than during the regular course of their business of dispensing or selling drugs at retail.

   A pharmacy's voluntary registration may provide FDA with information about the facility, such as its name, location, and ownership structure, but voluntary registration alone does not give FDA additional authority over the pharmacy. In fact, a compounding pharmacy might register with FDA to give the impression that the Agency provides a higher level of oversight or approval of the pharmacy's activities than it actually does.

The Honorable Gene Green

1. **During the first round of questions you said there are certain drugs that neighborhood compounders should not be making. Is that something FDA wants to be able to forbid with new authority?**

   Yes. With noted exceptions, certain products are not appropriate for compounding under any circumstances. These products include: 1) what are essentially copies of FDA-approved drugs, absent a shortage justification based on the drug appearing on FDA's shortage list; and 2) complex dosage forms such as extended release products; transdermal patches; liposomal products; most biologics; and other products as designated by FDA. Producing complex dosage forms would require an approved application and compliance with cGMP standards, along with other requirements applicable to manufactured drug products.

2. **Does FDA currently not have authority to regulate what drugs can be compounded?**

   FDA currently has some authority to regulate what drugs can be compounded. For example, under section 503A, FDA can, through rulemaking, establish a list of drugs that may not be compounded because the drugs or their ingredients have been withdrawn or removed from the market because the drugs or their ingredients "have been found to be unsafe or not effective." FDA can also establish a list of drugs that present "demonstrable difficulties for compounding that reasonably demonstrate an adverse effect on the safety or effectiveness" of the drug and, therefore, may not be compounded. However, due to the Ninth Circuit decision in Western States, this would not be a national standard. Furthermore, FDA's authority to regulate compounded drugs is more limited than our authority over conventional manufacturers and has been challenged in the past. And, as we have previously stated, our present authorities are not well-suited to appropriately and effectively regulating this evolving industry.

3. **Additionally, to clarify from earlier, you seemed to be saying that FDA did not currently have the capacity to address all of the oversight and it would like to cover compounders, is that correct?**

   As Dr. Hamburg noted in her testimony, we look forward to working with Congress to explore the appropriate funding mechanisms to support this work, which could include registration or other fees, as Congress has authorized and FDA has successfully implemented in other settings. Providing establishment and reinspection fees to help defray the cost of enhanced oversight would significantly improve the current oversight of compounders.

4. **FDA has said in the past that they did not have regulatory authority to further investigate NECC in advance of the outbreak. However, FDA has inspected 31 facilities since the outbreak. In your testimony, you outside several other incidents, including one in Texas, which were the result of unsanitary compounds, what else has changed that FDA believes it has inspection authority now, but did not previously?**

FDA's authority over compounding pharmacies is more limited but not non-existent. And the existing framework is not the right fit for effectively regulating outsourcers who compound drugs in advance of or without receiving a prescription for an individually identified patient.

The fungal meningitis outbreak has caused us to review our past practices with regard to our oversight of compounding pharmacies. Using a risk-based model, we identified 29 firms for priority inspections focused on their sterile processing practices. During these 29 inspections, in two instances, FDA identified secondary firms associated with the priority inspections, for a total of 31 films. While we are exercising our current authorities to protect public health, our authorities are still being challenged. Notably, even in light of recent events, and even though we are often working with the state inspectors, our investigators' efforts are being delayed because they are denied full access to records at some of the facilities they are inspecting. Just during the recent inspections, several pharmacies delayed or refused FDA access to records and FDA had to seek administrative warrants in two cases. And although we have been able to eventually conduct the inspections and collect the records that we have sought, our ability to take effective regulatory action to obtain lasting corrective action with regard to substandard sterility practices remains to be seen.

For example, FDA may inspect a pharmacy and find issues with that pharmacy's sterile processes, but, depending upon the facts of the case, may lack the authority to take legal action needed to ensure that the pharmacy corrects those issues.

5. **Have all of the compounders that you have inspected willingly opened their doors to FDA or, even in light of the recent tragedy, have there been some compounders that have challenged FDA's authority?**

As noted above, even though we are often working with the state inspectors, our investigators' efforts were delayed because, among other things, they were denied full access to records at some of the facilities they are inspecting. Just during the recent inspections, several pharmacies delayed or refused FDA access to records and FDA had to seek administrative warrants in two cases. And although we have been able to eventually conduct the inspections and collect the records that we have sought, our ability to take effective regulatory action to obtain lasting corrective action with regard to substandard sterile practices remains to be seen.

6. **I'd like to hear more on the specifics of how FDA will be able to use its new authority. Will it requires user fees or some other type of fee paid my compounders in order to facilitate this authority?**

As noted above, we look forward to working with Congress to explore the appropriate funding mechanisms to support this work, which could include registration or other fees, as Congress has authorized and FDA has successfully implemented in other settings. Providing establishment and reinspection fees to help defray the cost of

enhanced oversight would significantly improve the current oversight of compounders.

7. **Can we draw a bright line at whether the entity ships over state boundaries as the determining factor for 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?**

In response to Questions 7 and 8, under FDA's proposal, interstate shipment would be one of three factors that would subject certain compounders to Federal quality standards adequate to ensure that the compounding could be performed without putting patients at undue risk. The other two factors are 1) sterile compounding and 2) compounding in advance of or without receiving a prescription. Under our proposal, FDA could also exercise its authority to take action against any compounder that is, for example, making misbranded or adulterated products, making copies of FDA-approved drugs, or making certain products that should not be compounded under any circumstances. In addition, for all compounders, traditional and non-traditional, FDA should have clear ability to examine records such as records of prescriptions received, products shipped, volume of operations, and operational records such as batch records, product quality test results, and stability testing results. Such inspections are necessary to contain an outbreak or other public health threat, determine when a pharmacy exceeds the bounds of traditional compounding, and enforce the other provisions of the law.

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