THE FUNGAL MENINGITIS OUTBREAK: COULD IT 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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C O N T E N T S

[1] Mr. Cadden did not present a statement for the record.

THE FUNGAL MENINGITIS OUTBREAK: COULD IT HAVE BEEN PREVENTED?

WEDNESDAY, NOVEMBER 14, 2012

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

The subcommittee met, pursuant to call, at 10:04 a.m., in room 2123, Rayburn House Office Building, Hon. Cliff Stearns (chairman of the subcommittee) presiding.

Members present: Representatives Stearns, Terry, Murphy, Burgess, Blackburn, Gingrey, Scalise, Gardner, Griffith, Barton, Upton (ex officio), DeGette, Schakowsky, Castor, Markey, Green, Christensen, Dingell, and Waxman (ex officio).

Also present: Representative Whitfield.

Staff present: Sean Bunyun, Communications Director; Anita Bradley, Senior Policy Advisor to Chairman Emeritus; Karen Christian, Deputy Chief Counsel, Oversight; Debbee Keller, Press Secretary; Katie Novaria, Legislative Clerk; Andrew Powaleny, Deputy Press Secretary; Krista Rosenthall, Counsel to Chairman Emeritus; Alan Slobodin, Deputy Chief Counsel, Oversight; Peter Spencer, Professional Staff Member, Oversight; John Stone, Counsel, Oversight; Tom Wilbur, Staff Assistant; Phil Barnett, Democratic Staff Director; Tiffany Benjamin, Democratic Senior Counsel; Stacia Cardille, Democratic Deputy Chief Counsel; Brian Cohen, Democratic Investigations Staff Director and Senior Policy Advisor; Eric Flamm, Democratic FDA Detailee; Kiren Gopal, Democratic Counsel; Elizabeth Letter, Democratic Assistant Press Secretary; Karen Nelson, Democratic Deputy Committee Staff Director, Health; Stephen Salsbury, Democratic Staff Assistant; Rachel Sher, Democratic Senior Counsel; Roger Sherman, Democratic Chief Counsel.

OPENING STATEMENT OF HON. CLIFF STEARNS, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF FLORIDA

Mr. STEARNS. Good morning everybody, and the committee will come to order.

My colleagues, we convene this hearing of the Oversight and Investigations Subcommittee to examine the recent outbreak of fungal meningitis linked to contaminated products made by the New England Compounding Center, or NECC.

I want to extend my deepest condolences to everyone who has lost a loved one in this tragedy. Thirty-two people have died, including three within my congressional district, one in Marion

County. One of the persons lived right up the street from me. And well over 400 people have been sickened, making this one of the worst public health disasters ever caused by a contaminated drug in this country.

After a tragedy like this, the first question we all ask is, Could this have been prevented? After an examination of documents produced by the Massachusetts Board of Pharmacy and the U.S. Food and Drug Administration, the answer appears to be yes.

Before this outbreak, FDA had conducted three series of inspections of NECC, each based on a separate set of allegations or events. The Massachusetts Board of Pharmacy's history with NECC is even more extensive, involving at least 12 separate complaints concerning NECC or its pharmacist, Mr. Cadden, since NECC opened in 1998.

Over the course of these inspections, regulators noted the same kinds of problems at issue in the current outbreak, problems with sterility in violation of its own license. For example, back in 2002, several adverse events were reported to FDA involving patients who had received steroid injections made by the NECC. FDA followed up and inspected the company. Just 6 months after that inspection, patients were again hospitalized after receiving NECC's injections in what case can only be seen as a warning, just a simple warning of things to come. The patients infected in 2002 displayed meningitis-like symptoms. The product in question was the very same product connected to the current outbreak. In that case, the NECC drug was contaminated with bacteria.

After the 2002 meningitis cases, officials from FDA and the State pharmacy board met in 2003 to review NECC's conduct. Now, during this meeting, the FDA made a prophetic statement. The FDA stated that there was "the potential for serious public health consequences if NECC's compounding practices, in particular those relating to sterile products, are not improved."

Even though FDA was clearly aware of the risks posed by NECC's compounding practices, the agency was simply slow to act. In fact, it took FDA 4 years after finding problems with the NECC's sterility practices and violations of the Food, Drug and Cosmetic Act to issue a simple warning letter. The company challenged the charges FDA made in the 2006 warning letter. It took FDA another 2 years to respond to the company's claims. When FDA finally responded in 2008, 6 years after the agency first inspected the NECC, it directed the company to correct the violations and warned that it would follow up with future inspections. But the FDA never did so. FDA didn't even follow up after the Colorado Board of Pharmacy notified the agency in 2011 that the NECC was again sending its drugs to out-of-State hospitals without first receiving patient prescriptions. FDA didn't even refer this complaint to the Massachusetts board for follow up. We are left to wonder what would have happened if FDA had investigated or at least informed the Massachusetts Board of the Colorado of this complaint. It is possible that this outbreak very well might have been prevented.

My colleagues, we are joined today by Joyce Lovelace, whose husband, Eddie, passed away in September. Mrs. Lovelace, we sincerely thank you for sharing your story with us today. I pledge that

we will get to the bottom of this so we can ensure that this outbreak, things like this never ever occur again.

We are also joined by Commissioner Hamburg of the FDA and Commissioner Smith of the Massachusetts Department of Public Health. I am interested in learning whether they think this outbreak could have been prevented and whether their agencies did enough to stop it.

This committee has a long history of conducting bipartisan oversight, and this investigation is no exception. So it is my sincere hope that this hearing will serve and it is an opportunity to determine the reasons why such a history as this does not repeat itself.

[The prepared statement of Mr. Stearns follows:]

Opening Statement of the Honorable Cliff Stearns
Subcommittee on Oversight and Investigations
Hearing on The Fungal Meningitis Outbreak: Could It Have Been Prevented?
November 14, 2012
(As Prepared for Delivery)

We convene this hearing of the Oversight and Investigations Subcommittee to examine the recent outbreak of fungal meningitis linked to contaminated products made by the New England Compounding Center, or NECC.

I want to extend my deepest condolences to everyone who has lost a loved one in this tragedy. Thirty-two people have died—including three within my district in Marion County, Florida, one of whom lived right up the street from me—and well over 400 people have been sickened, making this one of the worst public health disasters ever caused by a contaminated drug in this country.

After a tragedy like this, the first question we all ask is: could this have been prevented? After an examination of documents produced by the Massachusetts Board of Pharmacy and the U.S. Food and Drug Administration – the answer here appears to be yes.

Before this outbreak, FDA had conducted three series of inspections of NECC, each based on a separate set of allegations or events. The Massachusetts Board of Pharmacy's history with NECC is even more extensive, involving at least 12 separate complaints concerning NECC or its pharmacist, Mr. Cadden, since NECC opened in 1998. Over the course of these inspections, regulators noted the same kinds of problems at issue in the current outbreak – problems with sterility and violations of its license.

For example, back in 2002, several adverse events were reported to FDA involving patients who had received steroid injections made by the NECC. FDA followed up and inspected the company. Just six months after that inspection, patients were again hospitalized after receiving NECC injections. In what can only be seen as a warning of things to come, the patients infected in 2002 displayed meningitis-like symptoms. The product in question was the very same product connected to the current outbreak. In that case, the NECC drug was contaminated with bacteria.

After the 2002 meningitis cases, officials from FDA and the state pharmacy board met in 2003 to review NECC's conduct. During this meeting, the FDA made a prophetic statement. The FDA stated that there was "the potential for serious public health consequences if NECC's compounding practices, in particular those relating to sterile products, are not improved."

Even though FDA was clearly aware of the risks posed by NECC's compounding practices, the agency was slow to act. In fact, it took FDA four years after finding problems with NECC's sterility practices and violations of the Food Drug and Cosmetic Act to issue a Warning Letter. The company challenged the charges FDA made in the 2006 Warning Letter. It took FDA another two years to respond to the company's claims. When FDA finally responded in 2008 - six years after the agency first inspected the NECC – it directed the company to correct the violations and warned that it would follow-up with future inspections. But FDA never did. FDA didn't even follow-up after the Colorado Board of Pharmacy notified the agency in 2011 that NECC was again sending its drugs to out-of-state hospitals without first receiving patient prescriptions. FDA didn't even refer this complaint to the Massachusetts Board for follow-up. We are left to wonder what would have happened if FDA had investigated, or at least informed the Massachusetts Board of the Colorado complaint. It is possible that this outbreak very well might have been prevented.

We are joined today by Joyce Lovelace, whose husband Eddie passed away in September. Ms. Lovelace, we thank you for sharing your story with us today. I pledge that we will get to the bottom of this so we can ensure that an outbreak like this never happens again.

We are also joined by Commissioner Hamburg of the FDA and Commissioner Smith of the Massachusetts Department of Public Health. I am interested in learning whether they think this outbreak could have been prevented and whether their agencies did enough to stop it.

This committee has a long history of conducting bipartisan oversight, and this investigation is no exception. It is my sincere hope that this hearing will serve as an opportunity to determine the reasons why so that history doesn't repeat itself.

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Mr. STEARNS. And with that, I give the remaining time to Chairman Emeritus Joe Barton.

Mr. BARTON. I think your time has expired, Mr. Chairman.

Mr. STEARNS. OK, well, then we will go to——

Mr. BARTON. If there is time at some point——

Mr. STEARNS. I think we will go to the ranking member, Ms. DeGette, who is recognized for 4 minutes.

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

Ms. DEGETTE. Thank you very much, Mr. Chairman. And I do appreciate your taking the time to have this hearing on the very day that we return from the recess because this is such an important public health issue, and we are acting in a bipartisan way. I am also glad about that.

The contaminated steroid injection sold by the New England Compounding Company have caused 438 cases of fungal meningitis spanning 19 States. Thirty-two people have died, and I am afraid that number could continue to climb.

We have four witnesses today to help us examine how this could have happened, and I am very eager to hear from the FDA and the Massachusetts Board of Registration and Pharmacy, the agencies with primary regulatory authority over NECC, just how we got here. I want to hear from Mr. Barry Cadden about how on Earth his company could have been so irresponsible causing the deaths of so many Americans. And I'm looking forward to hearing from Mrs. Lovelace, who, as you heard, is the wife of one of the first victims in this tragedy.

I want to join with Mr. Stearns, Mrs. Lovelace, in expressing my deep, deep sadness for your loss, and I really want to thank you today. It can't be easy.

And Congressman Whitfield, thank you so much for accompanying her today. I know this is hard for you, but it is important.

Mr. Chairman, the facts that we have uncovered so far in this investigation reveal frightening failures on multiple levels, and this is one of those real cases where there is a lot of blame to go around for a lot of people.

Mr. Cadden repeatedly failed to ensure that NECC and its sister companies were following appropriate safety rules and guidelines. Again and again, reports of problems with the facility were brought to the attention of the Massachusetts Board of Registration and Pharmacy, which failed to act. The board was informed of problems, via complaints or even from its own inspections, in 1999, 2002, 2003, 2004 and even just this past summer. But somehow, NECC was able to keep its license, avoid significant penalties and continue its operations until tragedy struck all across the Nation.

We also need to hear an explanation from the FDA. Just like the Massachusetts board, FDA inspectors and officials were repeatedly informed of problems at NECC, but the strongest action taken by the FDA was a warning letter sent to the company in 2006, a letter that appeared to have very little effect. The FDA tells us that they were hobbled by questions about whether they had the legal authority to address the problems at the NECC.

If this is true, Mr. Chairman, this is a problem that demands this full committee's immediate attention. We need to clarify the Food, Drug and Cosmetics Act, which apparently limits the FDA's jurisdiction over compounding pharmacies, and we need to make sure that for these large pharmacies like this, that they have the ability to act and to act quickly on behalf of patients.

Over 30 people have died from this meningitis outbreak because too many signals about the risk were missed. One of those signals, as the chairman said, came from my home State of Colorado. In 2011, the Colorado State Board of Pharmacy determined that NECC was distributing unlicensed and unregistered drugs in the State and issued a cease-and-desist order. But this was not all the Colorado officials could do, and it was not enough to stop NECC's action. Colorado officials notified the Massachusetts Board of Pharmacy, and Massachusetts did nothing. The Colorado Board of Pharmacy did the right thing, but the system failed. NECC did not improve its operation. The FDA did not act. And Massachusetts did not act.

Now, Mr. Chairman, for a long time, we have all had sort of a Norman Rockwell vision of the pharmacists who manufacture the drugs our families rely on, the kindly old gentleman in the white coat in the back of the store mixing the prescriptions for the little child with the illness. Unfortunately, this tragedy makes clear that large corporate compounding pharmacies are operating unchecked by appropriate safeguards, even as American families trust their lives. So we need to work together now, Mr. Chairman, to make sure this crisis is not repeated. And I will yield the remainder of my time to Mr. Markey from Massachusetts.

OPENING STATEMENT OF HON. EDWARD J. MARKEY, A REPRESENTATIVE IN CONGRESS FROM THE COMMONWEALTH OF MASSACHUSETTS

Mr. MARKEY. I thank the gentlelady.

New England Compounding Center is in my district in Framingham. My deepest condolences go to all victims and their families.

NECC was no stranger to Federal and State regulators. It had been the subject of eerily similar safety complaints in 1999, 2001 and 2002. Yet, in 2002, NECC's owner, Barry Cadden was appointed to the State's task force charged with developing new regulations for compounding pharmacies. And in June of 2006, the State board waived sanctions.

My report, which I have completed on this issue, shows that even before the current outbreak there were at least 23 deaths, 86 serious injuries associated with unsafe compounding pharmacy practices.

To Jerry Cohen, Melanie Norwood, and Joyce Lovelace, I want to commit to you and to all of the victims that I will not stop until we make sure that these industries are safe.

I thank you for your courage. We have to make sure that this never happens again.

I yield back.

Mr. STEARNS. Thank you.

The gentleman yields back.

I recognize the full chair of the committee, the distinguished gentleman from Michigan, Mr. Upton.

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

Mr. UPTON. Thank you.

You know, when we first began this investigation over a month ago, we knew that people were sick, and we knew that people had died and were dying due to contaminated medicine made by the New England Compounding Center.

One of my constituents, too, a grandmother from Cass County, lost her life tragically to these contaminated drugs.

The loss of innocent lives is tragic enough, but what makes this tragedy worse is the fact that it seems that these deaths and illnesses could have been prevented. The NECC was not unknown to its regulators. It was not operating under the shadow of darkness. The NECC plant is about a 30-minute drive from the FDA's New England District Office, and the FDA and NECC's State regulator, the Massachusetts Board of Pharmacy, had inspected NECC's facility a number of times since the company opened its doors back in 1998.

FDA even issued a warning letter to the NECC in 2006, and the Massachusetts Board of Pharmacy entered into a consent agreement with the company that same year.

I was stunned and angered to learn that inspection of the NECC by the FDA and the Massachusetts Board over 10 years ago identified contamination in the very same drug at issue in the current outbreak. The reason for that inspection? Patients had been hospitalized with meningitis-like symptoms. 10 years later, we are in the midst of an unthinkable worst-case scenario. The body count is growing by the day, and hundreds, hundreds have fallen ill. Inexcusable.

Today we are going to hear from the Massachusetts Department of Public Health and the FDA about their history and the NECC and why they treated the company the way that they did. Why did State and Federal regulators feel confident that this company could make drugs safely after repeatedly finding that the company's drugs were contaminated back in 2002? After observing multiple violations of the Food, Drug and Cosmetic Act leading up to the FDA's 2006 warning letter, why did the agency fail to conduct a single follow-up inspection?

The committee expects the cooperation of the FDA, the Massachusetts Board and the company as we try to uncover the facts as to ensure that this never happens again. Thirty-two innocent Americans have died during this outbreak, and the public deserves to know what went wrong. I thank Dr. Smith and Dr. Hamburg for agreeing to testify today. The Massachusetts Board in particular has provided thousands of pages of documents relating to the NECC.

Thank you, Dr. Smith, for making yourself and your staff available to the committee. I wish I could say the same about the FDA.

Commissioner Hamburg, the FDA still has not provided the key timeline information requested by the committee more than a month ago. The FDA has not provided its communications relating

to the NECC. FDA needs to focus on protecting public health by cooperating with its authorizing committee. We are going to insist today on a firm timetable from you as to when you can produce those documents and the rest of the requested information. The sooner that the FDA cooperates, the sooner we can determine what went wrong and what we need to do to fix it so it doesn't happen again.

Mrs. Lovelace, our hearts are with you. They really are. We appreciate your testimony during this very, very tough time, and I yield the balance of my time to Mr. Barton.

[The prepared statement of Mr. Upton follows:]

Opening Statement of the Honorable Fred Upton
Subcommittee on Oversight and Investigations
Hearing on The Fungal Meningitis Outbreak: Could It Have Been Prevented?
November 14, 2012
(As Prepared for Delivery)

When we first began this investigation just over a month ago, we knew people were sick and we knew people had died and were dying due to contaminated medicine made by the New England Compounding Center. One of my own constituents, a grandmother from Cass County, Michigan, sadly lost her life to the contaminated drugs.

The loss of innocent lives is tragic enough. But, what makes this tragedy worse is the fact that it seems these deaths and illnesses could have been prevented. The NECC was not unknown to its regulators. It was not operating under the shadow of darkness. The NECC plant is about a thirty-minute drive from the FDA's New England District Office. The FDA and NECC's state regulator, the Massachusetts Board of Pharmacy, had inspected NECC's facilities multiple times since the company opened its doors in 1998. FDA even issued a Warning Letter to the NECC in 2006. The Massachusetts Board of Pharmacy entered into a consent agreement with the company that same year. I was stunned and angered to learn that an inspection of the NECC by the FDA and the Mass Board over 10 years ago identified contamination in the very same drug at issue in the current outbreak. The reason for that inspection? Patients had been hospitalized with meningitis-like symptoms. Ten years later, we are in the midst of an unthinkable, worst-case scenario - the body count is growing by the day - and hundreds have fallen ill. This is simply inexcusable.

Today, we will hear from the Massachusetts Department of Public Health and the FDA about their history with the NECC and why they treated the company the way they did. Why did state and federal regulators feel confident that this company could make drugs safely, after repeatedly finding that the company's drugs were contaminated back in 2002? After observing multiple violations of the Food, Drug, and Cosmetic Act leading up to FDA's 2006 Warning Letter, why did the agency fail to conduct a single follow-up inspection?

The committee expects the cooperation of the FDA, the Massachusetts Board, and the company as we try to uncover the facts so as to ensure this never happens again. Thirty-two innocent Americans have died during this outbreak and the public deserves to know what went wrong. I thank Dr. Smith and Dr. Hamburg for agreeing to testify today. The Massachusetts Board, in particular, has provided thousands of pages of documents relating to the NECC. I thank you, Dr. Smith, for making yourself and your staff available to the committee staff as we investigate this outbreak. I wish I could say the same about the FDA. Commissioner Hamburg, the FDA still has not provided key timeline information requested by the committee over a month ago. The FDA has not provided its communications relating to the NECC. FDA needs to focus on protecting public health by cooperating with its authorizing committee. I want a firm timetable today from you on when you will produce your documents and the rest of the requested information. The sooner FDA cooperates, the sooner we can determine what went wrong and ensure we never endure a deadly outbreak like this one.

Mrs. Lovelace, I want to thank you for your testimony today during this very difficult time - we all are deeply saddened for your loss.

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OPENING STATEMENT OF HON. JOE BARTON, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF TEXAS

Mr. BARTON. Thank you, Mr. Chairman.

You have heard the old saying, you can bring a horse to water, but you can't make it drink. Well, you can take a regulator to a problem, but you can't make it regulate.

And we have got numerous cases in the last 10 to 15 years of State and Federal regulators being made aware of problems at this particular company, and they go out and investigate, or they ask for documentation, and then they issue some sort of a general reprimand or, in some cases, do nothing at all.

It is an absolute tragedy without any question that 32 people have died, and it is very unlikely that that is going to be the end of the death toll.

We have got to get our regulatory authority, both at the State and Federal level, when you have what appears to be a back bad actor like this company, you have got to get the regulators to use the authority that the States have given them and the Congress has given them to stop these practices.

And if you read the reports of both the majority and the minority staff that was prepared for this hearing, there are repeated instances of where an inspector just walking through could see obviously contamination in the various batches of this particular product, and it has been going on for 10 to 15 years.

So I want to thank Chairman Upton and Subcommittee Chairman Stearns and Ranking Member Waxman and DeGette for, on a bipartisan basis, immediately calling for this hearing, immediately asking that the facts be made present, and let's find out what the facts are and then do what is necessary to put a stop to this once and for all.

With that, Mr. Chairman, I yield back.

[The prepared statement of Mr. Barton follows:]

Opening Statement of the Honorable Joe Barton
Subcommittee on Oversight and Investigations, Hearing
"The Fungal Meningitis Outbreak: Could It Have Been Prevented?"
November 13, 2012

Thank you Mr. Chairman for holding this important hearing. Unfortunately, we sit here today to review the facts and figure out what could have been done differently to prevent the recent outbreak of fungal meningitis that has left 32 innocent people dead.

The contamination comes from an injectable steroid compounded and distributed by the New England Compounding Center (NECC). When you read the Committee Memo for this hearing and the recent media reports, you can't help but ask "how did this happen?"

For over a decade, the State of Massachusetts and the Food and Drug Administration (FDA) have been investigating and expressing concerns about the compounding practices at NECC. It appears that a perfect storm was forming. The facts indicate that the President of NECC, Barry Cadden, acted negligently and his facility was plagued with sterilization problems, the state and federal government received numerous complaints about the NECC and practiced a lot of bureaucratic hula-hooping, and ultimately they both failed to take formal action against the NECC in time to prevent this current catastrophe.

In Texas we have a saying, you can lead a horse to water, but you can't make it drink. Well the same is true in this situation. You can lead the regulators to a problem, but you can't make them regulate.

The public deserves answers from the NECC, the FDA, and the Massachusetts Department of Public Health, all of whom were invited to testify today, and this Committee will not stop our investigation until we get them.

Mr. STEARNS. The gentleman yields back.

I recognize the ranking member of the full committee, the gentleman from California, 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 very much, Mr. Chairman.

I want to thank you for holding this hearing and working with the Democrats in making this a bipartisan hearing. We are convening in the midst of an ongoing public health tragedy. The New England Compounding Center shipped across State lines over 17,000 vials of a steroid, an untold number of which were contaminated with a dangerous fungus, these injections have so far killed 32 people and sickened 438 people with meningitis. This is a tragedy that has brought unspeakable devastation to so many families.

That is why I'm very grateful, Mrs. Lovelace, for you being here today. It takes a lot of courage for you to come forward and speak about this, but it is important that you do so.

The facts that we have learned to date are very, very troubling. First of all, let's not lose sight of the wrongdoer as we go around blaming regulators. The regulators deserve blame, but the primary blame, in my mind, is the company. We had to subpoena the former President of the NECC, Barry Cadden, to be here to testify about how this company handled the matter. And what we learned was that even 10 years ago, people who are regulating the company found that there were sloppy practices that could lead to a public health problem. In fact, the FDA 10 years ago knew that there could be a possible meningitis outbreak, and it wasn't corrected by the company.

And the company went about its ways, I suppose always telling people that they are going to behave better, they are going to change their ways. Well, that doesn't mean we don't insist on regulators watching out for the public interest.

And I am pleased that both sides of the aisle are talking about the need for regulation, and what we need to do is straighten out who has what responsibility to be sure it is clear.

The Massachusetts Board of Registration and Pharmacy and other State regulators and health care providers identified the problem at the company. The Massachusetts Board inspected the facility after the outbreak. They found a horrifying list of problems, and it is shameful that those that ran this facility allowed this to happen.

The Massachusetts Board had primary jurisdiction, no one questions, that the State had primary jurisdiction to regulate the company. They were informed numerous times of problems. They even did their own investigation identifying serious issues, but the board never took actions tough enough to stop the New England Compounding Center from putting consumers at risk.

And finally, we have FDA. FDA was informed of the problems. They conducted investigations. They raised concerns about the NECC, but the most aggressive action the agency took was a warning letter in 2006. That letter and previous attempts by the FDA to inspect and review NECC's actions were met with stubborn re-

fusals and a challenge to FDA's authority. Well, the FDA is questioning their authority. Congress acted specifically in 1997 to limit the authority of the FDA and there was a Supreme Court case that left the FDA in doubt as to exactly the authority it had left.

This tragedy demands action from this Congress. Mr. Markey has a bill that is a good start. I think we want to work during this lame duck session to pass bipartisan legislation that preserves compounding pharmacies' abilities to operate safely in appropriate situations, yet gives FDA the clear and effective authority to prevent compounders from becoming dangerous drug manufacturers, like the NECC.

Mr. Chairman, I want to yield the balance of my time to Mr. Dingell.

Mr. STEARNS. The gentleman from Michigan is recognized for the balance of the time, but with the consent, unanimous consent, that you could have additional 2 minutes and we have additional two speakers that will speak each a minute a piece after you, if that is by unanimous consent accepted.

Mr. DINGELL. I'm not about to make it difficult, and I do thank you for the courtesy, Mr. Chairman.

Mr. STEARNS. With unanimous consent, so ordered.

And the gentleman, distinguished chairman emeritus of the full committee under the majority and the Dean of the House, is recognized 3 minutes.

OPENING STATEMENT OF HON. JOHN D. DINGELL, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF MICHIGAN

Mr. DINGELL. Mr. Chairman, I thank you for your courtesy. I commend you for holding this hearing, and I'm very pleased with the speed with which the committee has responded.

I ask unanimous consent to revise and extend my remarks, and I note that my home State of Michigan leads the country in the number of cases related to this fungal meningitis outbreak with 129 patients affected and 9 deaths. These individuals and their families deserve answers as to how this was able to occur. We also need to ensure our people that the pharmaceuticals that they purchase are safe. It is clear that the New England Compounding Center, which has a long history of sterility issues and significant other problems, was not properly regulated by either Federal or State authorities and that the sitting on the border between of the two authorities, they were able to disregard their responsibilities and lead us into a bad situation.

It is further clear that NECC blatantly chose not to address deficiencies and violations found by FDA and the Massachusetts Board of Pharmacy and additionally compounded these steroids without patient-specific prescriptions as required by Massachusetts State law.

While I recognize that compounding serves an important public health purpose, I am concerned that NECC was operating at such a volume as to be outside what may properly be considered traditionally pharmacy compounding and may instead be properly classified as a drug manufacturer and engaged in drug manufacturing.

Warnings were given on many occasions to all concerned, and we are going to have to see to it that that situation does not again obtain.

I would note that we have sort of the classic system of the tragedy of the commons before us, where what belongs to everybody or more than one appears to belong to no one, and as a result, neither agency responsible for its actions dealt with the problems.

I'm sure this committee hopes and intends to work with all of us together on both sides of the aisle to find out how new FDA authorities can address the issue before us with proper expansions of regulatory authority and what additional statutory authority may be needed to prevent future outbreaks like the one from which we are now suffering.

I am fearful, Mr. Chairman, that this problem is something which will require fairly strong legislation, but I'm satisfied it is fairly easily done.

I thank you for your courtesy to me, and I yield back the balance of my time.

Mr. STEARNS. I thank the distinguished gentleman and now recognize the gentleman from Virginia, Mr. Griffith, for 1 minute.

OPENING STATEMENT OF HON. H. MORGAN GRIFFITH, A REPRESENTATIVE IN CONGRESS FROM THE COMMONWEALTH OF VIRGINIA

Mr. GRIFFITH. Thank you, Mr. Chairman, and thank you so much for holding this hearing.

Like so many others who have spoken, my area in the Roanoke Valley and the New River Valleys of Virginia have been particularly hard hit. We have had two fatalities, and I was on the phone this morning with the father of the youngest victim to date in the United States, a young man who just turned 16 when he was stricken down. He has the advantages of age, but they don't know what his end result will be. On the Friday before he was stricken, he caught, as a sophomore, caught three interceptions in a football game, ran one back for a touchdown, just a great athlete, this gives him some advantages, but how will his life be changed? We don't know.

Our job here is to find out why this happened and then to make sure that it doesn't happen again. And I look forward to working with everyone to make sure that we get to the bottom of this in a bipartisan fashion and also want to thank Mrs. Lovelace for being here today and express sorrow for your loss.

With that, Mr. Chairman, I yield to Mrs. Blackburn.

Mr. STEARNS. The gentlelady from Tennessee is recognized for 1 minute.

OPENING STATEMENT OF HON. MARSHA BLACKBURN, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF TENNESSEE

Mrs. BLACKBURN. Thank you, Mr. Chairman, I am appreciative of the work that you and your staff have done and the manner in which we have moved forward so quickly on this issue.

And I do want to welcome our witnesses.

And Mrs. Lovelace, we do welcome you. We are appreciative that you would take your time to join us.

According to the CDC, 81 Tennesseans have been affected with fungal meningitis, and 13 Tennesseans have lost their life. This is something that is of tremendous concern to us, and it is because of this and on behalf of my constituents and those families that have been adversely impacted by this fungal meningitis outbreak, I am interested to hear why the FDA did not pursue any enforcement actions against NECC, despite having emphasized nearly a decade ago, nearly a decade ago, the potential for serious public health consequences. These are answers that we are looking for. They are questions that we have each approached during our comments, and I look forward to the hearing.

I yield back.

Mr. STEARNS. The gentlelady yields back.

We are now ready to have our first panel. Our first panel is Mrs. Joyce Lovelace. She is the wife of the late honorable Eddie C. Lovelace. Judge Lovelace served as a circuit judge for the 40th Judicial Circuit in Kentucky's Clinton, Cumberland and Monroe Counties.

Judge Lovelace was the first confirmed death as a result of the fungal contamination from steroid injections.

Before Mrs. Lovelace begins her testimony, I would like to recognize her congressman, the distinguished gentleman from Kentucky, who is also chairman of the Energy and Power Subcommittee and represents the First District of Kentucky, for an introduction of Mrs. Lovelace.

Mr. WHITFIELD. Chairman Stearns, thank you very much, and Ranking Member DeGette and all of the members of this committee.

We genuinely appreciate your being here to investigate this very important issue.

I feel very fortunate to be here with Joyce Lovelace today, not only because she is a constituent but because, ever since I have been a Member of Congress, Joyce and her husband, Eddie, have been very good friends of mine. They lived in Albany, Kentucky. We talk about statistics and figures, and yet when you look at the individual lives involved, it makes all the difference in the world.

Joyce and Eddie were married almost 56 years. He died on September the 17th, 2012, as a result of complications from the contaminated steroid injection that caused fungal meningitis and which is the focus of this hearing. He was 78 years old, but I might say that most people who met him thought he was 50 years old because he walked 3 or 4 miles every day. He was a circuit judge, was one of the leading legal scholars in Kentucky, had also served as a chief prosecutor, a county attorney, and he was one of those people involved in every aspect of the community of Albany. So we will all miss Eddie Lovelace, and we will never forget him.

And at this time, I want to thank Joyce very much for being willing to share her story and Eddie's story with the committee. And Joyce, thank you very much for being here with us this morning.

Mr. STEARNS. I thank my colleague for that fine introduction.

STATEMENT OF JOYCE J. LOVELACE, WIFE OF EDDIE C. LOVELACE

Mr. STEARNS. Ms. Lovelace, you are aware that the committee is holding an investigative hearing and when doing so has had the practice of taking testimony under oath.

Do you have any objection to testifying under oath?

Mrs. LOVELACE. No.

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

Mrs. LOVELACE. I'm fine.

Mr. STEARNS. In that case, if you are able to stand—if not, then please raise your right hand, and I will swear you in.

[Witness sworn.]

Mr. STEARNS. You are now under oath and subject to the penalties set forth in Title 18, Section 1001 of the United States Code. We welcome you today and your can now give your 5-minute summary opening statement if you would.

Mrs. LOVELACE. Thank you, Mr. Chairman and members of the committee. I'm very much encouraged by what I have heard from you today, that you do plan to move on this and to investigate this matter. That is basically what my family and I desire, is to get to the bottom of this and make sure that it never happens to another family because we have lived a nightmare. We will be living this nightmare for ages to come. It is something that probably we will never really be able to get closure because it was such a useless thing that happened to my husband.

I don't have any notes. My husband hated notes. Obviously, he can't be here, and I'm here on his behalf. So I'm just speaking from the heart, and I think he would not want me to have notes. He never read, he always spoke.

I was fortunate enough to have been married to this amazing man for nearly 56 years. And I won't say that it was always pleasant or smooth or anything, and I don't think any marriages are, but we worked together in his office. We were married when he was in law school. And I worked and helped him make his way through law school, and then we moved to Albany and made our home there. And he immediately began to get involved in civic matters, community matters. He taught Sunday school 42 years. He was still teaching when he passed away. He was a gifted speaker.

Really, I just want these people to know what kind of a person that has perished because of their lack of concern. My family is bitter. We are angry. We're heartbroken. We're devastated. And I just come here begging you to do something about the matter.

I cannot say enough good about him. He was bigger than life in any setting that you put him in. And I worked in his office alongside of him, so I've seen all sides and have seen him interact with all classes of people in all situations. And he had a gift of working with people. He was compassionate. He wanted to help the people that needed it. He always wanted the victim in any to be taken care of and given full consideration. And it's ironic that he winds up the victim in this.

Our family, I can't begin to tell you what I have lost, my soulmate, my partner, words don't, can't describe. Our older grandchildren. He was their anchor, their rock. They looked to him for advice. He guided the older ones through college and helped them decide what steps or what direction that they wanted to take. Our oldest granddaughter became an attorney based upon her appreciation I think for him and the work that he did. And he had 2 more years left in his term as judge. He planned to complete that term and go in practice with our granddaughter and help her get started. Now she has no one.

Our younger grandchildren have lost the best playmate they ever had. He played anything that our grandchildren asked him. They could dress him up. They could do anything, and he was happy to do it. They all wanted Papaw, our youngest granddaughter asked him, even when gas prices were so high, and they still are, asked him, you drive me around Pops and let me just read. And he would get her in the car, and he would drive and let her read her books. She is now in the sixth grade, and she is an avid reader. But these are some of the things that we are going to miss.

He had a very legal mind. He studied the law. Every weekend, on Friday, he wanted all the opinions of the appellate courts printed out and that was his weekends, reading. He would get kind of miffed at us if we didn't get it done because that would ruin his weekend.

Now he wasn't a sick individual. He was healthy. He walked 3 miles every morning before I would even get out of bed. He wanted to stay active. He didn't have the appearance of a 78-year-old man until about the second injection, and then we began to see the difference, for he had walked those streets every morning, he was stumbling, he was losing his balance, he fell often. He began to have headaches, which he never had before. And I was really concerned at his appearance. He had the look of someone who might have cancer. He had a physical examination just maybe 2 weeks before he fell sick, before he became sick, and they found nothing wrong. The only problems he had were kidney stones and allergies, neither of which I think would have taken his life.

On the 11th of September, he began to have numbness in his hand, and we begged him to go to the emergency room, and he declined. That evening, he had a bad headache, and then he told me that two fingers on his hand were not right. He couldn't use those two fingers. Then it became his fist; he couldn't. But he still would not go to the emergency room. He just was an individual that was not sick that much, and he wasn't going to go to doctors. He just didn't go until he had to.

The next morning, of course, he had been up, and when I got up, he was hollering for me in the kitchen. He had a horrible look on his face. I will never forget that expression. And he said, my legs don't work. He said, I've been out twice to get my paper, and I've fallen twice. Our daughter is a nurse, and I called her and she took him to the emergency room.

I believe they did a CT scan there, and it didn't show anything, but based on his symptoms they transferred him to the Vanderbilt in Nashville. To back up, he had had a car accident in March, the last of March and had injured his lumbar and cervical spine. And

he had gone through his physical therapy. He had done everything the doctors had told him to do in an effort to try to get better. To be able to work was number one on his mind, to get back on the job. He was transferred—he was referred to a Dr. Abrams, a neurosurgeon at St. Thomas, and that's where he received these injections at the St. Thomas Neurosurgical Outpatient Center. They admitted him to Vanderbilt on the 12th. He immediately, just within a day or two, started declining fast, I mean rapidly. His speech became slurred. He lost the use, he had no grip in his left hand. He could not move his left foot. He had no eye-hand coordination. He could not feed himself. It was a nightmare to see this man who was perfectly healthy one moment and then just so quickly going downhill, and everything the doctors were doing for him didn't—was to no avail. The medicine, whatever they did, it was not helping him in the least. And he just declined so rapidly, that on the 17th, he passed away.

And people, it was not an easy death that we witnessed. And these are human beings that these committees, the FDA, the NECC, whoever is responsible. I want them to know their lack of attention to their duties cost my husband his life, cost my family, caused them a loss that we will never recover from. And if you don't do your job, it may not appear to be anything to you, but you are affecting human lives, valuable human lives. My husband was valuable to us. And I cannot beg you enough, bipartisan, I don't care what party, work together——

Mr. STEARNS. We will do.

Mrs. LOVELACE. And please legislate this so no other family has to go through what we have.

[The prepared statement of Mrs. Lovelace follows:]

Mister Chairman and members of the United States House Energy & Commerce Committee.

My husband, Hon. Eddie C. Lovelace, died on the 17th day of September, 2012 as a result of fungal contamination from a series of epidural steroid injections which he received at the St. Thomas Outpatient Neurosurgical Clinic in Nashville, Tennessee. I want to express my thanks to this committee, members of the news media, lawyers and citizens who have diligently worked to bring light to one of our nations darkest healthcare secrets. This product was manufactured by the New England Compounding Pharmacy, Inc., d/b/a New England Compounding Center, located in Framingham, Massachusetts under the guise of compounding drugs. This company and many others operate with little or no regulation and in violation of both federal and state laws.

My husband devoted his life to public service and planned to serve as Circuit Judge for two more years and then re-enter the private practice of law with our granddaughter. Eddie Lovelace, at age 78, epitomized the senior citizens of our modern society who are determined to remain active and who have much to give to their community. To accomplish his continued active lifestyle, Eddie walked more than three miles a day, kept up on current events and remained a student of the law as he read every case being decided by our appellate courts.

The citizens of our community have lost a civic leader, a church leader, and outstanding judge. His near photographic memory, his booming voice, his sense of humor and his deep-seated concern for his fellow citizens led him to be a speaker at many civic and social functions and led him to frequently deliver eulogies of his friends who had preceded him death. His uncanny ability to quote Shakespeare, the Bible, poetry and famous quotations both entertained and brought comfort to many.

Words cannot describe the emotions that our family has undergone. Eddie's death was unexpected. When he first went into the hospital, the stroke was described as relatively mild with a good prognosis. Eddie was talking to friends and family and asking the doctors when he would be able to be back at work. Our optimism turned to despair in a few days when Eddie's health began to rapidly decline. On Monday following his stroke on Wednesday, we gathered in a hospital room at Vanderbilt University to do what no family wants to face - saying goodbye to a loved one. Eddie's 98 year old mother said goodbye to her "dear sweet boy" over the phone.

On Friday we buried Eddie and attempted to accept his death as natural. However, we kept going back over the fact that the doctor's were puzzled by the course his condition took. We were more puzzled when the St. Thomas Clinic called twice to inquire of Eddie's health and symptoms. Our suspicions were aroused. Finally, a newspaper reporter from the Tennessean called and told us that Vanderbilt was reporting that a 78-year-old male who died on September 17th was the first death associated with the fungal injections as a result of epidural steroid injections. We knew this must have been Eddie.

We searched for the truth knowing the truth would be difficult to accept. We asked our family friend and attorney, Thomas E. Carroll, to help us find the answers to our questions. Dr. George Nichols, II, retired Kentucky Chief Medical Examiner, advised an autopsy was the only way to get a definite answer. Dr. Nichols' autopsy confirmed that Eddie's death was a result of the fungal contamination from the epidural steroid injections. We now know that New England Compounding Pharmacy, Inc. killed Eddie. I have lost my soulmate and life's partner with whom I worked side by side, day after day for more than fifty years. Our children and older grandchildren have lost their friend, their advisor, and their anchor. The younger ones have lost their playmate. We are all left with sadness mixed with wonderful memories.

Every day as we read, watch TV and surf the internet we are confronted with the growing number of infections and deaths. More than 400 illnesses and more than 32

deaths are reported. Thousands awaken daily with the least amount of symptoms provoking fear and anxiety. At times our depression is temporarily replaced with anger. At other time it is replaced by determination and resolve.

Although I speak only for myself, I am sure that I echo the thoughts and wishes of every family that has been affected by this needless tragedy. I am asking this committee to find out how and why this happened and to plug the loopholes that allow these industries to escape meaningful inspection. If appropriate, I would ask that you refer this matter to the Justice Department to determine if federal laws have been broken. I would ask that you inquire how such a product became so widely distributed. Why did so many medical providers purchase this product from unregulated or poorly regulated sources? Don't just investigate. Instead, legislate and regulate. I challenge republicans and democrats alike to 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 Eddie Lovelace's public service continues even after death.

Respectfully submitted,

Joyce J. Lovelace

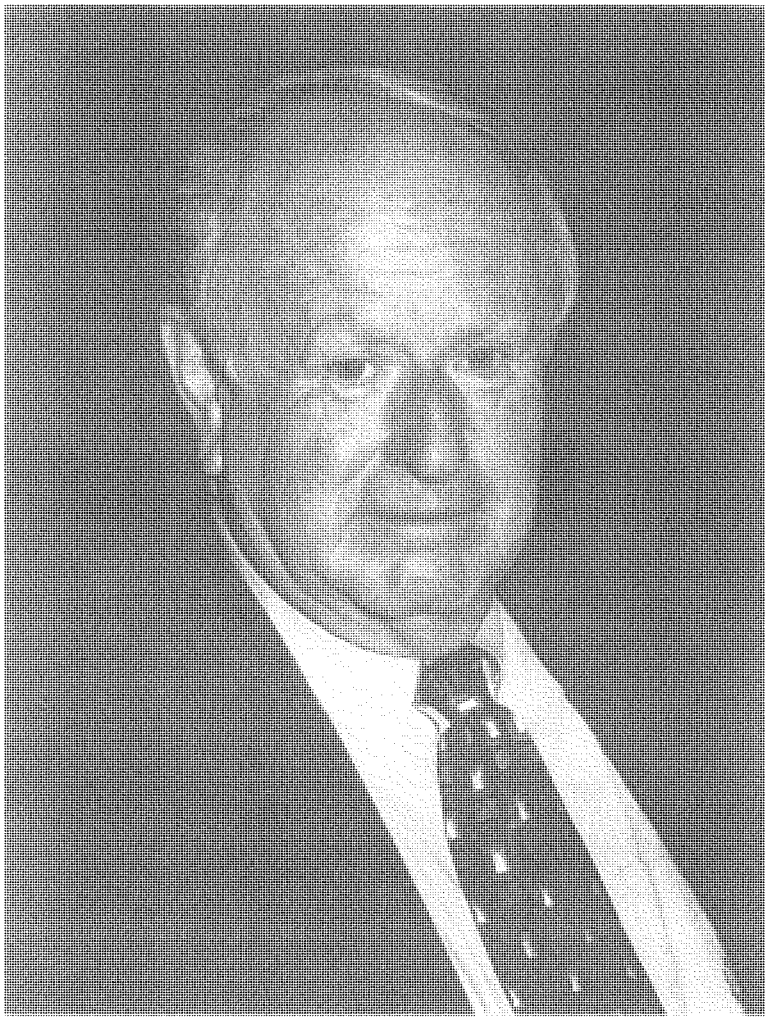
Attachments:
Death Certificate
CV of Hon. Eddie C. Lovelace
Photograph of Hon. Eddie C. Lovelace

Eddie C. Lovelace
Circuit Judge
40th Judicial Circuit
Clinton, Cumberland and Monroe Counties

- Born in Clinton County on February 9, 1934
- Received his B.A. from the University of Kentucky in 1956
- Received his J.D. from the University of Louisville in 1960
- Albany City Attorney 1961-1965
- Clinton County Attorney 1965-1969
- Commonwealth Attorney 1969-1992
- Circuit Judge Clinton, Russell & Wayne Counties 1992-2002
- Circuit Judge Clinton, Cumberland & Monroe Counties 2002-2012
- Outstanding Trial Judge of the Year 1995
- Member of UKAN Advocates of the University of Kentucky
- Member of Albany Lions Club for over 30 years, 5 of which he served as President
- Member of the Albany Masonic Lodge from 1972-1992 (Grand Master 1986, Deputy Grand Master 1987-1988, Grand Senior Deacon Grand masonic Lodge of Kentucky 1988-1989)
- Member of the Board of Directors, Lake Cumberland Area Development Council
- Kosair Shrine
- Lexington Consistory Scottish Rites
- Taught Adult Men's Sunday School at Albany First Baptist Church
- Received First Place in Kentucky State Speak Up Jaycee Contest
- Preceded in Death By:
    - Father, Amp Lovelace
    - Grandson, Elijah Christopher Lovelace

- Survived By:

    - Mother, Flonnie Lovelace
    - Wife, Joyce Davis Lovelace
    - Daughter, Karen Lovelace Talbott (Bob)
    - Son, Edward Christopher Lovelace (Carolyn)
    - Granddaughter, Megan Lovelace Thompson (BJ)
    - Granddaughter, Kristin Talbott DeRossett (Trevor)
    - Granddaughter, Kayla Rhea Talbott
    - Grandson, Edward Cory Lovelace
    - Granddaughter, Rhiannon Rashea Lovelace
    - Great-Granddaughter, Aubrey Caroline Thompson
    - Step-Granddaughter, Ashley Brook McGhee (Steven)
    - Step-Granddaughter, Nikki Danielle Upchurch
    - Step-Granddaughter, Taylor Renea Upchurch



Mr. STEARNS. Mrs. Lovelace, thank you very much for your poignant testimony, your statement.

I'm just going to ask two questions, short, brief. But the first one is, when you found out that your husband was the first of many to be linked to this contaminated product distributed by the NECC, do you remember when that was, how long after he died? And secondly, who was it that informed you about this?

Mrs. LOVELACE. He passed away on September the 17th, and we went ahead with the funeral services and everything, thinking that he had a stroke because that was their diagnosis. On the third of October, I believe it was, we began to hear about the contamination from these injections.

Mr. STEARNS. From the press? Who told——

Mrs. LOVELACE. Yes, through the press. My son-in-law, I think, was the first that read it or heard it. On October the 5th, I received a call from a reporter from the Nashville Tennessean, and he told me that a spokesperson at Vanderbilt had issued a statement that a 78-year-old man had died from the contaminated steroids.

Mr. STEARNS. So the first you heard about it was from the Vanderbilt hospital.

Mrs. LOVELACE. The first I heard that was from——

Mr. STEARNS. So no one from the FDA or the Center For Disease Control, did they ever contact you?

Mrs. LOVELACE. No. St. Thomas did not contact me.

Mr. STEARNS. So you actually heard about it through a press report?

Mrs. LOVELACE. Correct.

Mr. STEARNS. And no one from the State of Tennessee contacted you?

Mrs. LOVELACE. No.

Mr. STEARNS. Did they subsequently, after you heard through the press, did the State of Tennessee or FDA or the Centers for Disease Control?

Mrs. LOVELACE. I was on the Internet to try to find something about it, and I found a phone number on there, and I called it.

Mr. STEARNS. So you initiated it?

Mrs. LOVELACE. Yes.

Mr. STEARNS. No one from outside came to you?

Mrs. LOVELACE. No one.

Mr. STEARNS. Even after the press reports and the Vanderbilt Hospital, did the doctor call you?

Mrs. LOVELACE. No, but Vanderbilt didn't know about him having the injection. It was over at St. Thomas. Now, on the 25th—and bear in mind that his funeral was the 21st—on the 25th someone from St. Thomas called my cellphone and asked how Mr. Eddie was doing from his procedure. And I was really taken aback because we had just buried him. And I told her so. And well, she was so sorry; what happened? And I said, they believed he had a stroke. So then, the next day, a different lady from the same place called wanting to know what his symptoms were, how long he had the symptoms and whether or not we had an autopsy performed. And neither person mentioned contamination, meningitis, anything like that.

Mr. STEARNS. You know, it is a possibility what you say, a stroke, there might have been people that had died because of the contamination prior to your husband that were elderly and they attributed to a stroke.

Mrs. LOVELACE. It is very possible.

Mr. STEARNS. We will never know. I think my last concern is, is the feeling I have that you had no contact with the FDA and these other folks that I mentioned. I think if you, they did contact you, and told you about it, I think what you would say to them is, why didn't you stop it?

Mrs. LOVELACE. Right.

Mr. STEARNS. And obviously, if you had to talk to Mr. Cadden, who is the CEO of NECC, you could say, how in the world would you be so oblivious to the lack of quality control and all the notices that you got prior to your manufacturing of this large number of drugs? So those are the questions I want to ask you. I want to thank you again for your courage to come here, and I recognize the ranking member, Ms. DeGette from Colorado.

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

I just want to follow up, Mrs. Lovelace, on some of the things the chairman was saying, because when they went over to inspect NECC, they found vials with little black stuff in them, and they found insects near the areas and terrible, terrible working conditions. And you know, sometimes in this committee, we have seen this before with food manufacturers, and we all sit here and we say, "How could this happen in the 21st century in the most civilized country in the world?" And the reason why it is so important that you came today—and it is so hard for you, I am sure—is because it is easy for regulators and for Congress people to talk about this in the abstract and for every—for you being here, there are hundreds of people around the country who have either lost loved ones who were just as cherished to them as your husband was to you and—or they are sick and they are still sick.

So I just want to let you know, it makes a big difference for you to come here today. And I want to thank you for doing it. It is not easy, I know. And I also want to let you know that we are—with some of the food safety issues that we identified a few years ago, we actually did pass legislation that clarified it. And so as hard as this is and how senseless and unnecessary as this is, I will guarantee you that I will be working with Mr. Upton and the entire committee, Democrats and Republicans, to make sure we clarify this.

And I think one of the problems as well as just sloppiness on the part of the Massachusetts regulatory agency and the FDA, the other problem was this gray area in the compounding pharmaceutical law, where the FDA wasn't really sure if they had jurisdiction or they'd be sued in court. We can fix that, and I can guarantee you we will fix that. And when we do fix that, unlike these regulators, we will call you and let you know.

So thank you very much for coming, and I yield back the balance of my time.

Mr. STEARNS. The gentlelady yields.

We will open the floor for additional questions. Just to remind members the second panel is Barry Cadden, who is the CEO of NECC, as well as we have the third panel.

So would anyone like to ask a question? Mr. Burgess is recognized from Texas.

Mr. BURGESS. Thank you, Mr. Chairman.

And Mrs. Lovelace, I do appreciate your being here and sharing your story with us. You made the comment that your husband was important to your family. I just stress that he is important to this committee as well.

And just like the ranking member, when she was talking about some of the food safety investigation, we have done, your story, as you were relating it, was just so similar to, in this very room, maybe 2 years ago, we heard a similar story about salmonella, and the family actually learned about it, that the lost of their loved one, they learned about it through the newspaper that maybe it was the tomatoes in the salad or wherever the contaminant was from and the same thing, the place where things were grown, there were obvious areas where there was contamination going on.

We have read the memos, and we understand the litany of problems that existed at this manufacturer.

Can I just ask you a couple of questions to clarify in my mind the timeline that the clinical course that your husband had? He had the automobile accident, and roughly when was that?

Mrs. LOVELACE. March 30th of this year.

Mr. BURGESS. And then his treatment at the outpatient facility for the steroid injections, he had two of those.

Mrs. LOVELACE. Three.

Mr. BURGESS. Three. And so I guess the last one would have occurred when?

Mrs. LOVELACE. August 31st.

Mr. BURGESS. And his illness began.

Mrs. LOVELACE. The 11th, it really began before, but it was really magnified on the 11th.

Mr. BURGESS. So roughly not quite 2 weeks afterwards.

Mrs. LOVELACE. Uh-huh.

Mr. BURGESS. And when he was admitted to the hospital, when was transferred to Vanderbilt, when did that occur?

Mrs. LOVELACE. That was on the 12th, the morning of the 12th.

Mr. BURGESS. So he had a pretty rapid decline in his clinical course.

Mrs. LOVELACE. He did.

Mr. BURGESS. Did the doctors know in, coming into Vanderbilt, that he had had previous outpatient therapy at the other facility?

Mrs. LOVELACE. No, I don't believe they did. Our daughter accompanied him to the hospital, and I don't believe that that was in his history when he was admitted.

Mr. BURGESS. It may not have occurred to anyone to ask, and obviously, now, in retrospect, this all becomes very intertwined. This is tough, what you have been through; we don't have an opportunity to talk to them, but I suspect it is tough for the doctors involved as well——

Mrs. LOVELACE. I am sure it is.

Mr. BURGESS. For the doctors that provided the steroid injection, as well as the doctors that were treating, not knowing what they were up against.

Mrs. LOVELACE. I am amazed that they were ordering medicine from someone that had that reputation.

Mr. BURGESS. That is part of our problem, that information may not have gotten to where it needed to get.

Well, again, we appreciate your courage and your strength for being here, relating it to us today. It is an important part of this story, and I certainly look forward to what we can do for you in the future. Thank you.

Mrs. LOVELACE. Thank you very much.

Mr. STEARNS. Anyone else who wishes to ask a question? Anyone on this side? Short question.

Mr. MURPHY. Just a short comment here. I thank you for being here because of the statement you made about the importance of the organizations involved that are supposed to be inspecting. Clearly, there is a lot of information that they knew that this compounding pharmacy had problems. And whatever the issue was, as you are keenly aware, surely you have searched so many times, how could someone stop and say, it is not my job, it is not in my job description, it doesn't matter? It is so important that you hear—and I am sure it is difficult, I am sure it is tragic—but it is still, I thank you for having the energy for being here and help people put a face on this. There is a role of these agencies, and at no time should ever someone say, this is a gray area, I don't want to overstep the boundaries, because the fact that people did that ended up in a tragic loss. So I thank you for having the courage to be here and helping to put a face on it.

Mr. STEARNS. I thank the gentleman.

And with that, Mrs. Lovelace, thank you very much for your testimony.

Mrs. LOVELACE. You are welcome.

Mr. STEARNS. And we thank our colleague Mr. Whitfield for his time, too.

And with that, we will call up the second panel.

Mr. Cadden is asked to come to the desk.

Mr. Cadden, my understanding is that Mr. Cadden authorized his counsel to advise the committee that he will rely on his Constitutional right not to testify at today's hearing. I believe that this privilege should be personally exercised before the members as we have done in the past, and that is why we have requested that he appear today before us.

I request that, given the importance of his testimony, he reconsider his decision to invoke his Fifth Amendment rights, especially because the families of the people who have lost their lives after receiving a contaminated injection made by his company, the New England Compounding Center, those who are sick and those who have received injections, are waiting to see if they, too, will get sick, they deserve some answers today.

Mr. Cadden, I ask you to consider, to reconsider and tell this committee and the people watching this hearing how this tragedy has happened.

STATEMENT OF BARRY J. CADDEN, PRESIDENT, CO–OWNER AND DIRECTOR OF PHARMACY, NEW ENGLAND COMPOUNDING CENTER

Mr. STEARNS. Mr. Cadden, are you aware that the subcommittee is holding this investigative hearing and, in doing so, we have the practice of taking testimony under oath?

Mr. CADDEN. On advise of counsel, I respectfully decline to answer on the basis of my Constitutional right——

Mr. STEARNS. First of all, Mr. Cadden, you just need a yes or no for this question.

Mr. TERRY. Put the microphone on.

Mr. STEARNS. Put your microphone on. So we are just asking you basically, you understand we have the practice of taking testimony under oath. You understand that. And do you have any objection to testifying under oath?

Mr. CADDEN. No.

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

Mr. CADDEN. Yes, I do.

Mr. STEARNS. In that case, would you be so kind as to identify your counsel for our record.

Mr. CADDEN. Mr. Attorney Bruce Singal and Steven Ross.

Mr. STEARNS. And Mr. Steven Ross.

OK, Mr. Ross do you want to come and sit at the front here?

Mr. ROSS. We are fine.

Mr. STEARNS. At this time, we are going to swear you in. Please raise your right hand, and I will swear you in.

[Witness sworn.]

Mr. STEARNS. Thank you, Mr. Cadden.

I will recognize myself for the first part of the question.

Mr. Cadden, are you the one—are you one of the owners of the New England Compounding Center, or NECC, the company that distributed contaminated injectables to medical clinics, doctor's offices, and hospitals across this country?

Mr. CADDEN. On advice of counsel, I respectfully decline to answer on the basis of my constitutional rights and privileges, including the Fifth Amendment to the United States Constitution.

Mr. STEARNS. Mr. Cadden, 32 people have died, 400 people are infected, and scores of others who were injected with medicine your company compounded are waiting, holding their breath to see if they will get sick from the products you have made.

You have been the director of pharmacy at the NECC since it opened. You were responsible for ensuring that the products were safe and sterile. Mr. Cadden, what explanation can you give the families who have lost their loved ones and those who are gravely ill for the actions of your company?

Mr. CADDEN. Mr. Chairman, on advice of counsel, I respectfully decline to answer on the basis of my constitutional rights and privileges, including the Fifth Amendment to the United States Constitution.

Mr. STEARNS. The Massachusetts Board found that you released two lots of the injectable drugs at issue in this meningitis outbreak

before you received the lab tests as to whether the drugs were sterile. They also found black particulate matter within the injectables. The FDA found greenish-black matter in the vials.

Mr. Cadden, there is no question there was a massive failure of sterilization at your facility. For the sake of protecting the public health and preventing something like this from ever happening again and to provide some explanation to grieving families, can you please tell us what was the breakdown that led to the contamination and the meningitis outbreak?

Mr. CADDEN. Mr. Chairman, on the advice of counsel, I respectfully decline to answer on the basis of my constitutional rights and privileges, including the Fifth Amendment to the United States Constitution.

Mr. STEARNS. I now recognize the ranking member, Ms. DeGette, for questions.

Ms. DEGETTE. Mr. Cadden, we just heard from Joyce Lovelace. Joyce Lovelace's husband Eddie was the first one who was found to have died of fungal meningitis from one of your company's products. He was a judge. He was a husband of 56 years. He was a father, a grandfather. He was getting ready in 2 years to leave the bench so he could go into law practice with his oldest granddaughter.

And there are a number of other victims around the country now who have either died or become terribly ill as a result of your product.

And the chairman talked about some of the findings that they found just this year in your company, the greenish-black foreign matter inside the vials. There were also things like a leaking boiler next to the clean room that created a pool of water, which creates a breeding ground for bacteria; an air-conditioning system that turned off at night despite requirements that the clean rooms had a consistent temperature. Your own environmental monitoring program showed violative levels of bacteria and mold in clean rooms between January and September of this year.

When FDA inspectors looked at NECC's sister company, Ameridose, they found the same kind of thing. They reported that there were insects in or near areas where sterile products were packaged, stored, and manufactured. They even saw a bird flying inside an area where there are supposed to be sterile packages.

So I guess I would ask you—I would ask you, what do you say to all of these patients and all of these families that have been devastated—devastated by these contaminated products that your company has produced?

Mr. CADDEN. On advice of counsel, I respectfully decline to answer on the basis of my constitutional rights and privileges, including the Fifth Amendment to the United States Constitution.

Ms. DEGETTE. Mr. Chairman, I think it is clear that the witness does intend to exercise his Fifth Amendment rights, and, with that, I think I will not ask any more questions. We won't have any more on this side.

Thank you.

Mr. STEARNS. I thank the ranking member.

Let me be clear, Mr. Cadden. Again, are you refusing to answer the questions on the basis of the protections afforded to you under the Fifth Amendment to the United States Constitution?

Mr. CADDEN. On advice of counsel, I respectfully decline to answer on the basis of my constitutional rights and privileges.

Mr. STEARNS. Will you invoke your Fifth Amendment rights in response to all questions today?

Mr. CADDEN. Yes.

Mr. STEARNS. Then you are excused from the witness table at this time. But I would advise you that you remain subject to the process of the committee and that if the committee needs are such, then we shall recall you.

Mr. CADDEN. Thank you, Mr. Chairman.

Mr. STEARNS. Yes.

Now, my colleagues, we will call up the third panel.

My colleagues, we have on the third panel Commissioner Margaret A. Hamburg. Margaret A. Hamburg became the 21st Commissioner of Food and Drug on May 18th, 2009. Prior to assuming her role as Commissioner, Dr. Hamburg was a senior scientist at the Nuclear Threat Initiative. She also served as the Assistant Secretary for Policy and Evaluation in the U.S. Department of Health and Human Services and as commissioner of the New York City Department of Health and Mental Hygiene.

We also have the interim commissioner, Lauren A. Smith. Lauren A. Smith has been the interim commissioner of the Massachusetts Department of Public Health since October 25th, 2012. And prior to assuming that position, Dr. Smith served as the medical director and chief medical officer of the department.

Let me welcome you to the committee. And let me ask you, you are aware that the committee is holding an investigative hearing, and when doing so, it has had the practice of taking testimony under oath. Do either one of you have an objection to taking testimony under oath?

Ms. HAMBURG. No.

Ms. SMITH. No.

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

Ms. SMITH. No.

Ms. HAMBURG. No.

Mr. STEARNS. In that case, if you would please rise and raise your right hand, I will swear you in.

[Witnesses sworn.]

Mr. STEARNS. 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?

STATEMENTS OF MARGARET A. HAMBURG, COMMISSIONER, FOOD AND DRUG ADMINISTRATION, AND LAUREN SMITH, INTERIM COMMISSIONER, MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

STATEMENT OF MARGARET A. HAMBURG

Ms. HAMBURG. Mr. Chairman and members of the subcommittee, I am Dr. Margaret Hamburg, Commissioner of the Food and Drug Administration. And I am joined by Howard Sklamberg, Deputy Associate Commissioner for Regulatory Affairs.

Thank you for this opportunity to testify about the tragic fungal meningitis outbreak associated with an injectable steroid product distributed by NECC and for our safety concerns related to compounding and the legislation that is needed to prevent such incidents from happening again.

I want to begin by offering my deepest sympathies to the patients affected by this outbreak and their families. This event has had devastating effects on patients across the country, such as Eddie Lovelace, Judge Lovelace, many of whom were likely unaware that they were being treated with a compounded product not reviewed or approved by the FDA.

Our foremost goal is the protection of the health of the public. Since the onset of this outbreak, we have targeted FDA resources, from experts in our headquarters to inspectors and scientists in district offices and labs across the country, to do everything we can to stem the toll of this terrible event. Together with CDC and the States, we have sought to identify potentially contaminated products and ensure that they are removed from the market and do not reach patients. We have collected and analyzed hundreds of samples from the relevant firms, as well as from medical facilities and State and local agencies, to isolate the cause and determine the extent of the contamination.

We are working daily to ensure timely, clear, and accurate information is disseminated about the findings of our investigation, what products are affected, and what providers should do with any products still on their shelves. And we are working to alleviate existing drug shortages exacerbated by product recalls.

We have also been reviewing actions taken in the past with regard to NECC. From our review thus far, we have no reason to believe that any of the specific actions in question, a more timely issuance of the 2006 warning letter, or inspectional follow-up, would have prevented this recent tragedy.

What we do know is that stronger, clearer authority would enable more effective regulation of the drug-compounding industry, especially when it has been evolving so significantly. As it is, our authority over compounding is limited, unclear, and contested. And in the face of differing views in Congress and the courts about FDA's authority and continuing challenges by industry, the agency has struggled with how to chart an effective course to protect the public health.

We recognize that traditional compounding provides an important service for patients who, for example, can't swallow a pill or are allergic to an ingredient in a drug product. But the industry has evolved well beyond the neighborhood pharmacist. In par-

ticular, the movement by many hospitals to outsource pharmacy compounding has created a market for compounding operations that produce drugs that reach far larger numbers of patients. When these facilities operate well, they may serve an important function in terms of safety and efficiency. However, when they fail to follow safety and quality standards, many patients may be harmed.

Our best information is that there are thousands of other compounders out there producing what should be sterile products made to exacting standards, and, thus, many other firms with the potential to generate a tragedy like this.

The current oversight framework, in attempting to draw a bright line between compounders and manufacturers, fails to address the complex issues raised by a changing industry. Additionally, gaps and ambiguities in the law have hampered our ability to act to protect patients and to prevent rather than just react to safety concerns.

I am committed to working with Congress and other stakeholders to design a system of rational, risk-based regulation that takes into account both the Federal and the State roles. As I outlined in my testimony, we have developed a proposed framework that would tier the degree of oversight to the risk posed by the type of product and practices. Traditional compounding would remain the purview of the States. The higher risk posed by nontraditional compounding would be addressed by Federal standards, including standards for quality control.

And under this framework, certain products carrying the highest risk could not be compounded. They could only be produced by entities willing to meet the standards currently required of drug manufacturers.

We would like to explore with you authorities that would be important to support this new regulatory paradigm, including clear authority to access records, mandatory reporting of adverse events, additional registration requirements to facilitate appropriate oversight and coordination with State regulators, clear label statements to allow prescribers and consumers the opportunity to make informed judgments, and adequate funding to support the inspections and other oversight activities outlined in this framework.

And because a key piece of any plan involving oversight of pharmacy compounders will continue to be performed at the State level, we must work closely with our State partners as we develop the framework for new authorities. Consequently, FDA will be inviting representatives from all 50 States to participate in a full-day meeting on December 19th to facilitate these important discussions.

We have a collective opportunity and responsibility to help prevent future tragedies. If we fail to act, this type of incident will happen again. It is a matter of when, not if. If we fail to act now, it will only be a matter of time until we are all back in this room, sadly, asking why more people have died and what could have been done to prevent it.

I am happy to answer any questions you may have.

Mr. STEARNS. I thank you.

[The prepared statement of Ms. Hamburg follows:]

DEPARTMENT OF HEALTH & HUMAN SERVICES

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

"THE FUNGAL MENINGITIS OUTBREAK: COULD IT HAVE BEEN PREVENTED?"

NOVEMBER 14, 2012

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 the tragic fungal meningitis outbreak associated with compounded methylprednisolone acetate (MPA), a steroid injectable product distributed by the New England Compounding Center (NECC), and to discuss more broadly safety issues related to pharmacy compounding.

I want to begin by offering my deepest sympathies to the patients affected by this outbreak and their families. This outbreak has had devastating effects on individuals and families across the country. The Centers for Disease Control and Prevention (CDC) has reported 32 deaths among 438 individual cases (428 cases of fungal meningitis and 10 cases of peripheral joint infections)[1] across 19 states. Approximately 14,000 patients may have received injections with MPA from three implicated lots. In addition, two other NECC products have been found to be contaminated with different bacteria. We have found no adverse health effects to date from these additional products, but continue to investigate the public health implications of this contamination.

Although the investigation is ongoing, we want to provide you with an update on the actions that FDA has taken, and is continuing to take, to respond to this outbreak. We also want to suggest

[1] 428 cases of fungal meningitis, stroke due to presumed fungal meningitis, or other central nervous system-related infection meeting the outbreak case definition, plus 10 peripheral joint infections (e.g., knee, hip, shoulder, elbow).

steps that Congress can take to strengthen FDA's authority to help prevent tragedies like this from happening in the future.

FDA'S RESPONSE TO THE CURRENT OUTBREAK

FDA's primary goal since the onset of this outbreak has been to protect the public health. With the state and Federal partners, we are conducting thorough investigations of the relevant facilities, monitoring the voluntary recalls associated with these products to ensure that contaminated and potentially contaminated product is off of the shelves, and ensuring that information is communicated promptly and clearly to health care professionals and patients.

Let me briefly summarize the sequence of key events regarding the outbreak. On September 25, 2012, CDC notified FDA that it was working with the Tennessee Department of Health to investigate a cluster of meningitis cases at a single clinic, which might be associated with product contamination. When we learned of the potential contamination, we joined CDC in investigating. On September 26, NECC began a voluntary recall of three implicated lots of MPA and voluntarily ceased manufacturing of MPA. The Massachusetts Board of Registration in Pharmacy, which has primary oversight responsibility for pharmacies in its State, oversaw the recall, and initiated a one-day inspection of NECC's Framingham, Massachusetts, facility. FDA also began to coordinate with the Massachusetts Board of Registration in Pharmacy to plan for inspection of NECC. We coordinated closely with the State on this adverse event inspection, because the State has authority to compel certain actions where our authority is more limited.

FDA and the Massachusetts Board of Registration in Pharmacy initiated a joint inspection of NECC on October 1, 2012. On October 4, FDA and CDC held a joint press conference announcing the investigation of the meningitis outbreak.[2] On October 5, after FDA had observed fungal contamination by direct microscopic examination of foreign matter taken from a sealed vial of MPA collected from NECC, FDA issued a MedWatch Safety Alert to 220,000 health professionals to notify them of the fungal contamination. Out of an abundance of caution, the Safety Alert took the additional step of recommending that health care professionals and consumers not use any product produced by NECC. FDA also requested that health care professionals retain and secure all remaining products purchased from NECC until FDA provided further instructions about how to dispose of these products. In addition, the Safety Alert encouraged health care professionals and patients to report to the Agency's MedWatch Safety Information and Adverse Event Reporting Program any adverse events or side effects related to the use of these products. On October 6, at FDA's recommendation, NECC agreed to recall all products.

As our investigation continued, on October 11, we announced our findings showing the presence of a fungal contaminant in multiple sealed vials of MPA injection, made at the NECC's Framingham, Massachusetts, site. CDC confirmed the specific type of fungus related to the patient disease – *Exserohilum* – in this briefing as well.[3] On October 15, based on FDA's ongoing investigation and out of an abundance of caution, we further advised health care professionals to follow up with patients who were administered any NECC injectable product on

[2] "CDC and FDA Joint Telebriefing on Investigation of Meningitis Outbreak" (October 4, 2012); transcript available at *http://www.cdc.gov/media/releases/2012/t1004_meningitis_outbreak.html.*
[3] "CDC, FDA, Massachusetts Department of Public Health: Joint Telebriefing Updating Investigation of Meningitis Outbreak" (Oct. 11, 2012); transcript available at *http://www.cdc.gov/media/releases/2012/t1011_meningitis_outbreak.html.*

or after May 21, 2012, including an ophthalmic drug that is injectable or used in conjunction with eye surgery or a cardioplegic solution. After working closely with the State on October 22, the Agency made available two lists of customers (consignees) who received products that were shipped on or after May 21, 2012, from NECC's Framingham, Massachusetts, facility, advising those customers to check their stocks to identify whether they had any products from NECC, and if so, to immediately isolate any identified product from their drug supplies and contact NECC to obtain instructions on how to return products.

On October 26, FDA released a copy of the FDA Form 483 (list of observations made during the onsite inspection) issued to NECC. FDA observed, and has since confirmed, that contaminated products were made at NECC's Framingham, Massachusetts, facility, and listed a number of observations made during the course of the inspection regarding conditions in the clean room at this facility.

Most recently, on November 1, FDA and CDC laboratories announced that bacteria had been identified as present in three separate lots (batches) of NECC-supplied, preservative-free injectable betamethasone, with each lot producing different culture results (identifying different contaminants), and in a single lot of NECC cardioplegia solution. FDA stated that although final laboratory results on additional samples were still pending, the previous finding of fungal contamination of MPA and recent finding of bacterial contamination of injectable betamethasone and cardioplegia solution reinforced the Agency's concern about the lack of sterility in products produced at NECC's compounding facility and served to underscore that hospitals, clinics, and health care professionals should not use any NECC-supplied products.

The Agency has been working closely with CDC, numerous state health departments, and the Massachusetts Board of Registration in Pharmacy to investigate the outbreak of fungal meningitis. This is a far-ranging investigation across the United States. FDA, in conjunction with our state partners, is in the process of inspecting several facilities associated with this outbreak. This includes compounders, wholesale distributors, active pharmaceutical ingredient (API) suppliers, contract laboratories, and others. The Agency's first priority has been to detect any contaminated or potentially contaminated products, to prevent them from reaching U.S. consumers by ensuring they are effectively recalled and removed from the market, and, as discussed more fully below, to communicate key information about these products to the providers and patients who need it. In connection with this investigation, FDA has collected and analyzed hundreds of samples from firms associated with this outbreak, as well as from medical facilities and state and local agencies. In addition to staff at FDA headquarters, staff in FDA district offices in New England, New York, Dallas, Seattle, Chicago, Los Angeles, Detroit, Cincinnati, Kansas City, and Florida, and laboratory personnel in Denver, San Francisco, Atlanta, New York, and Boston, are assisting in this investigation.

FDA also inspected Ameridose LLC's facility in Westborough, Massachusetts as part of the Agency's ongoing fungal meningitis outbreak investigation. Ameridose and NECC share some of the same management. Ameridose entered into a voluntary agreement with the Massachusetts Board of Registration in Pharmacy to temporarily cease all pharmacy and manufacturing operations starting on October 10, 2012. After FDA's preliminary inspectional findings raised concerns about a lack of sterility assurance for products produced at and distributed by

Ameridose's Westborough facility, the company voluntarily recalled all of its unexpired products in circulation. FDA completed its inspection on November 9, 2012.

FDA is currently conducting recall audit checks of NECC's customers. In an audit check, FDA contacts a subset of the firm's customers, which in this case were health care facilities, to confirm that they received notice of the recall and took the action requested in the recall notice. In this case, the facilities were instructed to immediately segregate and quarantine the material and to work with NECC to coordinate return of the products. As of November 5, 2012, FDA had completed 587 audit checks of NECC's health care facility customers. FDA found no product remaining for use at any of the NECC customers that it audited, and all customers had knowledge of the recall. Ameridose commenced its product recall on October 31, 2012; FDA initiated its audit check process for the Ameridose recall on November 5, 2012.

FDA has identified six Ameridose products that were on the FDA drug shortage listprior to the recall (sodium bicarbonate injection; succinylcholine injection; atropine sulfate injection; bupivacaine hydrochloride injection; lidocaine hydrochloride injection and furosemide injection).

These six drugs were in shortage before the Ameridose shutdown due to manufacturing problems, delays, and discontinuations by commercial manufacturers. FDA's Drug Shortage Program is using every tool available to work with manufacturers to address these shortages. For five of the drugs, we expect the shortages to decrease based on all of the ongoing efforts of FDA and the manufacturers to address these shortages and do not anticipate the Ameridose shutdown to create additional issues. For sodium bicarbonate injection, we are continuing all efforts to

address the shortage, including exploring temporary importation to assist with supplies until demand is being met by the U.S. manufacturers.

FDA has communicated throughout this investigation with the media, Congress, state health officials, health care professionals, and the public to keep them apprised of important findings and developments as we move forward in our investigation. FDA's website is updated on a frequent basis to provide broad access to any new public information. This information is being further disseminated through the Agency's electronic listserves and through Twitter and Facebook. Along with CDC, FDA is providing health care professionals with information they need on an ongoing basis, and as new information comes to light, to advise and treat patients affected by this situation.

Targeted alerts have been sent to 150 health care professional organizations, including the national specialty-specific societies that work with spinal injections, such as the American Society of Anesthesiologists, the American Academy of Physical Medicine and Rehabilitation, and the North American Spine Society, and also to all state medical, pharmacist, nursing, and physicians' assistant societies, as well as all state boards of pharmacy. Regular phone updates are provided to state health departments, in collaboration with CDC, and written updates are also distributed to national pharmacy and ophthalmology professional organizations. FDA also contacted patient and health care professional groups and consumer groups and worked with the American Hospital Association as part of our response.

FDA pharmacists are fielding calls from the public and we have extended their hours of availability for the last several weeks to help respond to the public's concerns. We also continue to respond to calls and e-mails from health care professionals, hospitals and clinics, and others with questions about the NECC and Ameridose recalls.

The far-ranging investigation is ongoing and FDA will continue to update stakeholders as quickly as possible as information becomes publicly available.

FDA's past activities with respect to NECC include: a 2002 inspection in response to adverse event reports (followed by a State inspection and action under Massachusetts' authority) and a 2006 Warning Letter focused on lower risk issues associated with copying approved drugs, marketing and packaging. Throughout this time, NECC has repeatedly disputed FDA's jurisdiction over its facility.[4] The Massachusetts Board of Pharmacy reinspected NECC in 2011 in response to a letter from the firm indicating that NECC was "updating its facility and moving into adjacent space"; that inspection included a tour of the facility, security review, licensing review, and inspection of NECC's sterile and non-sterile processing areas.[5] The Massachusetts Board of Pharmacy inspection found the facility to be "Satisfactory."[6]

FDA'S LEGAL AUTHORITY OVER COMPOUNDED DRUGS

[4] Inspection Report for April 2002 inspection, at pp. 2, 3, 5; Establishment Inspection Report for 2002/2003 inspection, at p. 11; Inspection Memorandum for 2004 inspection, at p. 3; Warning Letter Response, at pp. 3-4

[5] A copy of MABRP's May 24, 2011, Inspection Report for NECC is available on MABRP's website at *http://www.mass.gov/eohhs/docs/dph/quality/boards/necc/03-new-england-compounding-pharmacy-incnew-england-coumpouding-center-inspection-report.pdf.*

[6] See MABRP's May 24, 2011 Inspection Report for NECC, id., at p. 10

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. Or it may involve making a suspension or suppository dosage form 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 1990's, 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.[7] In May 1996, in a House Commerce Committee hearing on FDA reform legislation, FDA Commissioner David

[7] 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

Kessler testified that the compounding provision being considered by the Committee was likely to encourage large-scale manufacturing under the guise of pharmacy compounding, and could allow for potentially dangerous compounding of sterile products, leading to serious safety problems or death.[8]

In November 1997, S. 830, the Food and Drug Administration Modernization Act of 1997 (FDAMA) was signed into law as Public Law 105-115.[9] FDAMA added to the FD&C Act's Section 503A, which addresses FDA's authority over compounded drugs.[10] Section 503A exempts compounded drugs from three critical provisions of the FDCA: the premarket approval requirement for "new drugs"; the requirement that a drug be made in compliance with current good manufacturing practice (cGMP); and the requirement that the drug bear adequate directions for use, providing certain conditions are met. These conditions include, among other things, that the compounding be performed by a licensed pharmacist or physician, that there be a prescription for the compounded product for an individual patient, and that the compounded product be necessary for an identified patient. It allows FDA to restrict the compounding of certain categories of drugs (after notice-and-comment rulemaking), and limits the quantity of compounded drugs that a pharmacy could ship out of state to five percent of the total prescription orders, unless the state enters into a Memorandum of Understanding with FDA that addresses the distribution of "inordinate amounts" of compounded drugs out of the state, and the handling of complaints about compounded products shipped out of the state. Section 503A also contains restrictions on the advertising or promotion of the compounding of any particular drug, class of

[8] Statement by David A. Kessler, M.D., Commissioner of Food and Drugs, Dept. of Health and Human Services, before the Subcommittee on Health and Environment, Committee on Commerce, House of Representatives (May 1, 1996).
[9] 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*
[10] Id.

drug, or type of drug, and on the solicitation of prescriptions for compounded drugs from prescribers. 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 authority over compounding pharmacies. We look forward to working with Congress to address these issues.

Looking Ahead

FDA believes that there is a legitimate role for traditional compounding to provide needed drugs to patients that, for example, need a drug that is allergen free or have a medical need that cannot be met with an approved FDA product. However, we have grown increasingly concerned about certain compounding practices, and we have seen an increasing number of incidents related to compounded drugs. The NECC/meningitis situation is the latest, and most serious, incident. As described above, 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. 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 prescription or order for an individual patient who has a documented medical need for the compounded drug.

Further, we recommend that the statute recognize 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 plays an important role in the health 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 based on one or more of the factors identified below. Non-traditional compounding would be subject to Federal standards adequate to ensure that the compounding could be performed without putting patients at undue risk. For example, enforcement could be by the FDA or by a State willing to effectively oversee the compounding activities, as determined by FDA.

Factors that could place a product into the "non-traditional compounding" category might include some statutorily-specified combination of: the type of product/activity (e.g., sterile compounding); the amount of product being made; whether the production is being done before

the receipt of a prescription or order for a particular patient (so-called "anticipatory compounding"); whether the compounded drug is being shipped interstate; or whether the drug is being dispensed to someone other than the ultimate user when it leaves the facility where it was produced.

Non-traditional compounding should, because of the higher risk presented, be subject to a greater degree of oversight, with the riskiest products subject to the highest level of controls, such as appropriate current good manufacturing practice ("cGMP") standards established by FDA. 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 cGMPs, along with other requirements applicable to manufactured drug products. We would seek to permit the Secretary to have sufficient flexibility in this area to make these exceptions necessary to address issues of public health.

FDA would like to explore with Congress other authorities that would be important to support this new regulatory paradigm. For example, FDA should be given clear, full authority 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 have clear statutory 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.

FDA also believes that pharmacies engaged in non-traditional compounding should register with FDA so that FDA can maintain an accurate inventory of such pharmacies to facilitate appropriate oversight and coordination with State regulators. In addition, FDA would like to explore with Congress several other ideas such as clear label statements identifying the nature and source of the non-traditionally compounded product, and requiring non-traditional compounders to report adverse events. The labeling statements would provide prescribers and consumers with valuable information about the products they are using or taking so that they can make informed judgments about their use. Requiring non-traditional compounders to report adverse events, as drug manufacturers are required to do, would allow FDA and the States to identify trends and to proactively take steps to curtail dangerous compounding practices. Other appropriate regulatory and enforcement tools might also be useful. Funding will be necessary 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 implemented in other settings.

In light of growing evidence of threats to the public health, the Administration urges Congress to strengthen Federal standards for non-traditional compounding. Such legislation should

appropriately balance legitimate compounding that meets a genuine medical need with the reality that compounded drugs pose greater risks than those that are evaluated by FDA for safety and efficacy and subject to manufacturing controls to ensure consistently high product quality. We recommend that it recognize the appropriate State role in regulation of traditional compounding, while authorizing Federal standards and oversight for non-traditional compounders that produce riskier products. We look forward to working with Congress in striking the right balance.

CONCLUSION

Protecting Americans from unsafe and contaminated drugs is not just an important responsibility of FDA—it is part of our core mission. To fulfill our mission, we must be able to proactively identify dangerous practices before they result in actual harm, and when necessary, intervene to minimize the damage and to prevent future similar events. Tragically, there have been 32 deaths to date associated with this outbreak. However, we are hopeful that our actions thus far and the ongoing investigation are preventing unknown numbers of further deaths, which might have occurred had we and our partners not acted aggressively after we became aware of the outbreak.

We look forward to working with Congress on legislation that will balance the need to allow legitimate forms of traditional pharmacy compounding with the need for adequate Federal oversight of higher risk pharmacy compounding practices.

I am happy to answer questions you may have.

Mr. STEARNS. Dr. Smith, for your summary of your opening statement?

STATEMENT OF LAUREN SMITH

Ms. SMITH. Thank you, Chairman Stearns, Ranking Member DeGette, and members of the committee. Thank you very much for having me here today. My name is Dr. Lauren Smith, and I am the interim commissioner of the Massachusetts Department of Public Health.

I have to also begin by saying that my thoughts are with the victims and families affected by this tragic outbreak and with Mrs. Lovelace, whose moving testimony only strengthens my resolve to ensure that no other family has to suffer what she aptly described as the heartbreak that hers has. As a mother, a pediatrician, and a public health leader, I have devoted my life and career to protecting the health of others. These events evoke in me the same sense of outrage as they do for you and the rest of the public. For many of you, I know this hits very close to home.

For the past 2 months, our department, along with the FDA, has conducted a joint investigation of New England Compounding Center, the source of this devastating fungal meningitis outbreak that has sickened hundreds and killed 31 people across the country. We have also investigated and shut down NECC's sister company.

NECC knowingly disregarded sterility tests, prepared medicine in unsanitary conditions, and violated their pharmacy license, endangering thousands of lives as a result. NECC bears the responsibility for the harm that they have caused with these actions.

I was given the responsibility, as interim commissioner, less than 3 weeks ago to lead my department through this crisis, and, like you, I have been trying to put together the pieces of the puzzle.

First licensed by Massachusetts in 1998, NECC and its owner, Barry Cadden, have since been the subject of numerous complaints, resulting in a series of investigations by the State and the FDA. These investigations led to the Board of Pharmacy's proposed reprimand and probation in 2004. This proposal was inexplicably weakened in 2006, allowing NECC to continue to operate without disciplinary actions, pending an independent evaluation of its progress under a consent agreement. The Board of Pharmacy's failure to take decisive disciplinary action in 2006 on these complaints has contributed to these tragic events.

In April of 2006, the Board of Pharmacy's staff learned that the principal of PSI, the evaluator for NECC, had been convicted of Federal crimes that resulted in 18 people being blinded. However, the staff did not share this information with board members before they accepted the report from PSI validating NECC's compliance with the consent agreement. These same staff members failed to act on a July 2012 report from the Colorado Board of Pharmacy that NECC had violated both Colorado and Massachusetts pharmacy regulations. These staff have been removed from their jobs.

Poor judgment, missed opportunities, and a lack of appropriate action allowed NECC to continue on this troubling path. We acknowledge that these lapses—some of which were preventable, but all are unacceptable.

From the early days of this outbreak, our department has acted swiftly and decisively. We secured a surrender of NECC's license, shut down its operations, and forced a total recall of all NECC products. We moved to permanently revoke NECC's license as well as the licenses of the three principal pharmacists who oversaw their operations. We also secured the suspension of operations of Ameridose and Alaunus, two other drug manufacturers owned by Barry Cadden, which, as you know, have been found to have similar substandard practices.

While taking these strong and necessary actions, we have reexamined our own State regulations regarding compounding pharmacies. Although our regulations are comparable to those in most States, they need to be strengthened to address the realities of this evolving industry.

On November 1st, Massachusetts enacted a series of emergency regulations to bring greater scrutiny to this industry and require sterile compounding pharmacies to report both volume and distribution information to us. Licensed pharmacies will also have to report when they are the subject of any State or Federal investigations. We have also begun unannounced inspections of all sterile compounding pharmacies in Massachusetts. Teams are conducting these inspections even as we speak.

To further strengthen our oversight over sterile compounding pharmacies, we must explore changes to the law. We have created a special commission to review best practices in other States and to identify stronger mechanisms for oversight for these pharmacies in Massachusetts.

As we work to raise standards in our State, we urge Congress to act to strengthen Federal oversight. Congressman Markey's leadership on this issue is laudable and would address some of the regulatory black holes that exist between State and Federal oversight.

As a pediatrician who has cared for acutely ill children and their families for almost 20 years, I must say that I understand the trust that patients place in our healthcare system. We must use these tragic events as an impetus to work together—public health leaders, public health officials, and legislators—to institute reforms to restore this trust and to ensure that something like this does not ever happen again.

We will keep the victims and their families always in our thoughts—they are not numbers, they are not statistics, but real people with real lives—as we work to identify responsibility and to implement policies and practices that can be effective and lasting.

Thank you. I appreciate the committee's interest in this matter, and I am grateful to you for acting so swiftly to have us come here to discuss it.

[The prepared statement of Ms. Smith follows:]

Testimony of Dr. Lauren Smith, Interim Commissioner
Massachusetts Department of Public Health

House Committee on Energy and Commerce
Subcommittee on Oversight and Investigations

United States House of Representatives
November 14, 2012

Good morning,

Chairman Stearns, Ranking Member DeGette, members of the Subcommittee, thank you for having me here today. My name is Dr. Lauren Smith, I am the Interim Commissioner of the Massachusetts Department of Public Health and I welcome the opportunity to have this discussion.

I want to say from the outset that my thoughts are with the victims and families affected by this tragic outbreak. As a mother, a pediatrician, and a public health leader, I have devoted my life and career to protecting the health of others. Have no doubt that these events invoke in me the same outrage that you and the rest of the public feel. The natural first question we all ask is "How could this possibly have happened?" The necessary second question is "What can we do to ensure that this terrible situation does not happen again?"

For nearly two months, our Department has conducted a joint investigation of New England Compounding Center (NECC), alongside our federal partners at the Food and Drug Administration (FDA), to answer these questions.

NECC is a Framingham, Massachusetts-based pharmacy that compounds sterile medications. It was identified as the source of the devastating fungal meningitis outbreak that has sickened hundreds and led to dozens of deaths across the country. For many of you, and for those with cases among your constituents in particular, I know these losses hit close to home.

NECC knowingly disregarded sterility tests, prepared medicine in unsanitary conditions and unlawfully engaged in manufacturing, endangering thousands of lives as a result. NECC bears the primary responsibility for the harm they have caused with these actions.

I was given the responsibility as interim commissioner less than three weeks ago, to lead my department during this crisis. And like you, I have spent the last several weeks trying to put together the pieces of this troubling puzzle.

Although the majority of these events happened in the previous administration and well before I came to the Department, I offer the following chronology based on a review of documents and reports from the time.

Let me begin by noting that by statute, the Massachusetts Board of Registration in Pharmacy, supported by the Department of Public Health's Division of Health Professions Licensure, has primary responsibility for oversight of the practice of pharmacy in the Commonwealth.

The Board of Pharmacy is an independent body, with 11 members appointed by the Governor. The Board has the responsibility and legal authority to license and regulate pharmacies and pharmacists. DPH staff investigators, lawyers, administrators, and an executive director support the Board's operations.

The Massachusetts Board of Registration in Pharmacy's interaction with NECC began on July 16, 1998, when it obtained its initial license. On February 2, 1999, the Board received the first complaint against NECC, which alleged that the pharmacy had provided a prescriber with pre-printed prescriptions that specifically listed NECC medications. State law prohibits pre-printed prescriptions. Prescriptions are required to be patient-specific, and based upon the patient's diagnosis, medical history, allergies, tolerance, and the specific constellation of symptoms that the patient is presenting. This complaint was resolved in October 1999 with an informal reprimand letter, a non-disciplinary action.

In April 2002, working with the FDA, the Board visited NECC and obtained records related to a recent MedWatch report concerning betamethasone, a compounded steroid suppository. The FDA investigator met with Barry Cadden, owner of NECC, and conducted an inspection on April 9, concerning procedures, sterility and record keeping.

In October 2002, the Board initiated a joint investigation with the FDA at NECC related to the April 2002 betamethasone complaints as well as MedWatch reports associated with the use of methylprednisolone acetate, the injectable steroid medication implicated in this current outbreak. The MedWatch reports pertained to two patients who received the steroid and experienced pain and headaches and were hospitalized with meningitis-like symptoms. Laboratory tests from these investigations identified subpotency of betamethasone and superpotency of methylprednisolone acetate. The FDA also noted contamination of one lot of methylprednisolone acetate with bacteria. These investigations continued into 2003.

Also in 2002, Board of Pharmacy member Karen Ryle convened a Task Force to study Board oversight of the compounding pharmacy industry. Barry Cadden

served on this Task Force, which met for nearly two years. The Task Force discussed proposals to change regulations around compounding, but records do not show whether formal recommendations were made, and the Board did not adopt new regulations.

In February 2004, the Board conducted a follow up inspection of NECC and noted that all deficiencies surrounding sterility, safety, quality and procedures from the 2002-2003 investigations had been resolved. Just weeks later, however, the Board received a complaint, from a pharmacist in Wisconsin, expressing concerns with the safety of a topical anesthetic product. The complaint alleged that NECC advised the pharmacy to unlawfully use a staff member's name rather than an individual patient's name in filling a prescription. The Board then in place resolved this complaint with a disciplinary warning letter on September 30, 2004.

Based on this series of investigations, in September 2004, the Board voted unanimously to sanction NECC with a reprimand, a three-year probation, and a requirement that Barry Cadden obtain additional training in sterile compounding. NECC objected to these sanctions, but the Board reaffirmed this approach through an additional unanimous vote on November 23, 2004.

More than a year later, on January 10, 2006, NECC entered into a non-disciplinary consent agreement with the Board that was significantly weaker than the earlier version. The signed consent agreement stipulated a one-year probation to be stayed with the condition that NECC hire an independent evaluator. The Board's staff identified Pharmaceutical Systems, Inc. (PSI) as the evaluator to conduct inspections of NECC's compounding practices.

Despite interviews with Board and staff members involved with these decisions and a thorough review of the limited records retained from this period, troubling questions remain about what influenced the more lenient consent agreement resolution, given NECC's track record. I will not be satisfied until we know the full story behind this decision.

What we know now is that from January to April 2006, the independent evaluator PSI conducted an assessment of NECC's compliance with United States Pharmacopeia Standards, and oversaw development of policies and procedures. PSI also issued recommendations for process improvement and provided training for NECC staff. An April 7, 2006 report from PSI described NECC's compliance with the evaluation.

Our investigation has revealed that in late April 2006, some Board of Pharmacy and Health Professions Licensure staff, including the Board's executive director and legal counsel, learned that PSI executives were convicted of federal crimes related to defrauding the FDA and selling unapproved sterilization equipment to hospitals. However, we have found no evidence to indicate that the Executive Director or staff attorney of the Board provided this crucial information to the

Board. Nor did they see fit to send inspectors back to NECC in 2006 to determine if they were fulfilling the requirements of the corrective action plan.

In May 2006, the Board voted to affirm that NECC was in compliance with the terms of the consent agreement, thus accepting PSI's findings in overseeing NECC's compliance.

Consistent with Board policy at the time, which was to inspect pharmacies only upon a change in licensure status or upon receipt of a complaint, the next time a Board investigator returned to the pharmacy was five years later on May 24, 2011 to inspect NECC following its renovation and expansion. This inspection included a full review of the facility space, operations, sterility protocols, and compliance with United States Pharmacopeia among other factors. The inspector found no evidence to suggest that NECC was violating patient-specific prescription requirements, and no deficiencies were cited.

In March 2012, the Board received a complaint pertaining to an insufficiently potent eye anesthetic distributed by NECC. This complaint focused on the potency of the medication but did not reference sterility concerns. This investigation continues.

In July 2012, some of the same staff members who failed to inform the Board of the issues surrounding PSI received a report from the Colorado Board of Pharmacy documenting violations of Colorado and Massachusetts pharmacy laws. The information provided to the Board executive director and legal counsel by Colorado showed that NECC had distributed bulk shipments of drugs to many hospitals in that state between 2010 and 2012 without patient–specific prescriptions, in violation of NECC's Colorado and Massachusetts licenses. The Colorado Board of Pharmacy issued a cease and desist order to stop NECC from engaging in the unlawful distribution of prescription drugs in the state in April 2011. Colorado informed the FDA of the adverse action, and provided them with the report, supporting evidence, and copy of the order. However, there is no record of Colorado providing similar notice to the Board or DPH.

Colorado contacted Board staff in July 2012 because NECC was violating the April 2011 cease and desist order by continuing to prepare and dispense bulk shipments without patient-specific prescriptions. However, after receiving the July report, both the executive director and legal counsel failed to order an investigation, inform the Board of the complaint, or take any other action on the Colorado complaint.

The first two lots of contaminated methylprednisolone acetate linked to the meningitis outbreak were prepared in May and June of 2012. The Colorado report was received two weeks prior to the production and shipping of the third lot of contaminated vials, which were prepared in August. Though issues of contamination with NECC products were not included in the Colorado report,

given NECC's history and the evidence from Colorado that the company was violating Massachusetts pharmacy regulations, prompt action was warranted.

The individuals responsible for this failure to act have been removed from their jobs. These steps are consistent with the swift and decisive actions of DPH since we became aware of the outbreak.

Late in the evening of September 24th, the Tennessee Department of Health notified our Department about a cluster of six exceedingly rare fungal meningitis cases. All six cases shared common risk factors, including an epidural injection of a steroid prepared by NECC. The Massachusetts DPH secured a list of medical facilities in 23 states that had received shipments of the steroids from three suspect lots identified by the Centers for Disease Control and Prevention. A day later, we secured a recall of those three lots, totaling 17,676 vials, and began our on-site investigation at NECC.

On October 1st, we were joined on-site at NECC by the FDA and commenced our joint investigation. Among a list of troubling findings, investigators observed visible black particulate matter in sealed vials that had been returned to NECC through the recall. Several batches of the drugs had been shipped by NECC prior to the completion of internal sterilization tests. Investigators also found evidence that NECC had been dispensing medication in bulk shipments rather than filling a patient-specific prescription for each dose dispensed.

We secured a surrender of NECC's license, shut down its operations and issued a total recall of NECC products.

Our aggressive investigation not only focused on NECC, but also companies with shared ownership. On October 10, we secured the voluntary suspension of operations of Ameridose, a Westborough, Massachusetts drug manufacturer also owned by Barry Cadden. This closure allowed for a full investigation by DPH and the FDA, and eventually led to a total recall of Ameridose products. Ameridose remains closed as the investigation continues.

The Board of Registration in Pharmacy moved to permanently revoke NECC's license, as well as the individual licenses of the three principal pharmacists who ran NECC so they may never practice pharmacy in Massachusetts again. The Board also issued a cease and desist order to all pharmacy staff at NECC to bar them from any compounding activities.

While taking these forceful and necessary actions, we have also reexamined our own approach to regulating this industry.

It is clear that the compounding pharmacy industry has changed drastically from the days of neighborhood businesses that served a local clientele. We

recognized that our state regulations needed to be strengthened to address the realities of this industry, which has evolved over time, and again we took action.

On November 1, Massachusetts enacted a series of emergency regulations to bring greater scrutiny to the industry and ensure that we have the tools to prevent such a tragedy from happening again.

Our new regulations stem from the lessons learned from this tragedy and require sterile compounding pharmacies in Massachusetts to report volume and distribution figures to the state, for the first time. This will alert us to any pharmacy that is acting like a manufacturer by producing medication on an industrial scale, which requires an FDA license and the additional scrutiny and adherence to high manufacturing standards for safety and quality that FDA oversight requires. We are also requiring all licensed pharmacies to report to the state when they are the subject of investigations by any other states or the federal government. This will allow us to know when other entities have identified issues with pharmacies in Massachusetts, including other states that issue non-resident licenses to pharmacies in Massachusetts.

The Board of Pharmacy's prior approach to inspecting pharmacies when they first apply for a license, and then again only if they move or if there is a complaint, though not out of line with the approach used by most states, is no longer sufficient to keep pace with the changing nature of the industry. Since the outbreak we have begun unannounced inspections of the state's 25 sterile compounding pharmacies to review how they function when they are not aware that an inspection is scheduled. Teams are in the process of conducting additional inspections as we speak.

Massachusetts sterile compounding pharmacies have also been required to attest under penalty of perjury that they are meeting all state laws and regulations.

To further strengthen our oversight over sterile compounding pharmacies, we need to explore changes to state law. We created a Special Commission, and named Christian Hartman, an expert in pharmacy practice and patient safety, as its chairman. The Commission will include members of the Massachusetts' Legislature and experts in pharmacy practice, regulatory affairs, and patient safety. We will look at best practices in other states, explore new ideas, and consider the interplay between state and federal authority. The first meeting of the Commission is scheduled for this month and this body will report its findings to the Governor by December 31.

As we work to raise standards in Massachusetts, we urge Congress to act to strengthen federal oversight. It is clear that the patchwork of disparate state regulations is not enough to keep the public safe.

Congressman Markey's leadership in putting forward legislation is laudable and would help fill what he has aptly called a "regulatory black hole" that exists between state and federal oversight. Congressman Markey's report also shows that at least 34 states have had deaths or illnesses stemming from violations at compounding pharmacies nationwide before this current meningitis outbreak. We join Congressman Markey in supporting immediate federal action.

As a pediatrician who has looked into the faces of children and families at their most vulnerable moments, I understand the faith and trust that patients place in our health care system. I would never have contemplated that a medicine I might prescribe to my patients could actually be the source of such harm. We must use these terrible events as an impetus to work together, as public health officials and legislators, to reaffirm the trust that has been broken by the circumstances surrounding this outbreak.

I pledge to you that Massachusetts will continue to do whatever we can, make any changes, and identify any areas of new law to make sure something like this never happens again. We intend to identify responsibility but also focus on reforms that will be effective and lasting.

As the victims and their families remain always in our thoughts, we accept the challenge of reform that lies ahead.

Thank you. And I am happy to take your questions.

Mr. STEARNS. Thank you, Dr. Smith.

Commissioner Hamburg, the title of this hearing is "The Fungal Meningitis Outbreak: Could It Have Been Prevented?"

Now, your testimony is 16 pages long. There is one sentence on FDA oversight on the New England Compounding Center prior to the outbreak. Now, this was—this is an investigative hearing. This was a complete and utter failure on the part of your agency and—Dr. Smith in her testimony admitted—and the State Board of Pharmacy. The committee's memorandum that we did, we had 25 pages laying this out. Yet you devoted just 1 sentence of your 16 pages in your opening statement that even talked about this oversight.

Over the years, the FDA repeatedly—repeatedly documented numerous problems at the NECC. Many of these problems are similar, if not identical, to the same problems which caused this outbreak. The agency ultimately issued a warning letter in 2006, 6 years ago, stating that if the company did not alter its practices, FDA would seize its product or issue an injunction and effectively shut down NECC.

Now, we heard Dr. Smith; you heard her testimony this morning. She talked about the mistakes they made and what they are going to do to correct it. You are here with your opening statement, you are practicing plausible deniability is what you are practicing.

When FDA issued the 2006 warning letter, did FDA have the authority to do what it said—namely, seize the drugs and shut down the committee—the company? Yes or no?

Ms. HAMBURG. I think it is important—the fact is——

Mr. STEARNS. No, the question is, did you have the authority——

Ms. HAMBURG [continuing]. The one letter did not involve sterility failures, and it was not in relation to the kinds of problems that we are addressing now.

Mr. STEARNS. So you are saying your letter was an empty threat?

Ms. HAMBURG. You know, I think one of the great challenges——

Mr. STEARNS. No, the real question is, did you think you had the authority——

Mr. WAXMAN. It wasn't her letter.

Ms. DEGETTE. It wasn't her letter.

Mr. STEARNS. Well, not your letter, personally, but——

Ms. HAMBURG. I think it is important to understand that I was not at——

Mr. STEARNS. No, I understand that and I appreciate that.

Ms. HAMBURG [continuing]. The FDA at the time and that——

Mr. STEARNS. And I am just staying that the frustration we have is——

Ms. HAMBURG [continuing]. The warning letter and the inspection it was based on had to do with a different set of complaints than sterility failures——

Mr. STEARNS. Let me rephrase the question. Do you think the FDA had the authority to shut down NECC? Yes or no?

Ms. HAMBURG. I think that is a very, very complex question and that the legal framework——

Mr. STEARNS. So you can't answer that question now?

Ms. HAMBURG [continuing]. For FDA activities is——

Mr. STEARNS. OK, let me ask another question.

Ms. HAMBURG [continuing]. Very, very unclear——
Mr. STEARNS. If you are not going to answer this question——
Ms. HAMBURG [continuing]. Contested, and limited.
Mr. STEARNS. [continuing]. Let me ask you——
Mr. WAXMAN. May she answer the question?
Mr. STEARNS. Well, she is not answering the question, Mr. Waxman.
Mr. WAXMAN. She is trying.
Mr. STEARNS. Well, I had asked her "yes or no," and she won't answer the question.
Ms. DEGETTE. She can't.
Mr. STEARNS. This is my—my questions can be asked. You can ask your question.
Ms. HAMBURG. You know, I think that the answer to your question is that, even on much smaller regulatory actions, the FDA authority to act was contested. Even going into NECC to do that inspection in 2004——
Mr. STEARNS. OK. Let me interrupt you——
Ms. HAMBURG [continuing]. We did not get access to the records immediately.
Mr. STEARNS. I am asking the questions, and I only have so much time.
You issued the letter in 2006. You said you were going to shut it down if they didn't improve on their quality assurance. Was that an empty threat?
Ms. HAMBURG. The——
Mr. STEARNS. Did the FDA think they had the jurisdiction, they had the responsibility to shut it down?
Ms. HAMBURG. The warning letter concerned, first and foremost, an issue that had to do with making copies of a commercially available drug.
Mr. STEARNS. We have a different interpretation——
Ms. HAMBURG. It was a different issue.
Mr. STEARNS [continuing]. Of my question. Let me interrupt you and ask you another question.
When the FDA inspected the NECC in 2002—that is 10 years ago—there was evidence that people had been infected by contaminated NECC products. Some of those people were experiencing meningitis-like symptoms.
What proof did the company provide then that it had corrected these problems?
Ms. HAMBURG. Well, as I think you understand from the documents we provided and the information that has been discussed, it was—we went in and we found problems, and we worked closely with the Massachusetts Board of Pharmacy to address them. But it was determined that the primary responsibility for overseeing NECC was Massachusetts because they were operating as a compound pharmacy——
Mr. STEARNS. So you were deferring to the State of Massachusetts?
Ms. HAMBURG. Well, we worked with the State. We——
Mr. STEARNS. OK.
Ms. HAMBURG [continuing]. Tried to provide help and assistance.
Mr. STEARNS. All right.

Ms. HAMBURG. But the responsibility for assuring——

Mr. STEARNS. So it is not your job; it is the State of Massachusetts'. OK.

Ms. HAMBURG [continuing]. Compliance with sterility issues was, in fact——

Mr. STEARNS. Let me ask this last question.

Ms. HAMBURG [continuing]. Not our direct responsibility.

Mr. STEARNS. Before the current outbreak, the last time FDA inspected the NECC was in January of 2005, which led to the warning letter. The warning letter stated that FDA may conduct follow-up inspections to ensure that the NECC was in compliance.

There was not a single follow-up inspection that occurred after 2005; is that correct? Yes or no?

Ms. HAMBURG. That——

Mr. STEARNS. Do you want me to repeat the question? There was not a single follow-up inspection that occurred after 2005.

Ms. HAMBURG. We did not do——

Mr. STEARNS. OK.

Ms. HAMBURG. Again, I have to——

Mr. STEARNS. OK. That is a "yes."

Ms. HAMBURG [continuing]. Make clear that I was not present——

Mr. STEARNS. All right, let me finish.

Ms. HAMBURG [continuing]. At the FDA at the time.

Mr. STEARNS. After noting——

Ms. HAMBURG. And it is my understanding——

Mr. STEARNS. OK.

Ms. HAMBURG [continuing]. And I cannot speak——

Mr. STEARNS. OK.

Ms. HAMBURG [continuing]. To all of the issues that were involved there, but——

Mr. STEARNS. You are taking my time. Let me finish.

After noting violations upon violation—violations upon violation in 2002 through 2005, why did the FDA feel confident that the NECC would correct its violations and obey the law? I mean, you had from 2002 to 2005 all these violations. What made you think that they would correct them? And not you, personally; I understand you weren't there.

Ms. HAMBURG. With respect to the first violations concerning the sterility issues, those were very serious concerns. We acted aggressively, in partnership with the State of Massachusetts.

But the day-to-day responsibility for overseeing the practice and remediating the sterility failures were taken on by the State of Massachusetts, who had the primary day-to-day oversight of this compounding pharmacy. A consent decree was reached in 2006, and we had understood, as had the Massachusetts Board of Pharmacy, that they were appropriately addressing those sterility concerns.

We had gone in in relation to a different complaint from a company about the copying of an FDA drug. And in that instance—we went in in relation to the manufacture of a specific product, trypan blue—it was not an issue of sterility failure or the conditions in the facility, but it was a practice that we felt they should not be pursuing, and that was what we were trying to address.

Mr. STEARNS. My time has expired, and I recognize the ranking member from Colorado, Ms. DeGette.

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

Dr. Hamburg, I want to try to clarify what is going on here, so I would appreciate short answers also.

Now, most of the FDA inspections into this manufacturer, NECC, were about 10 years ago, correct? And that was under the FDA under the Bush administration, correct?

Ms. HAMBURG. That is correct.

Ms. DEGETTE. OK. Now, in 1997—I was actually here then—the FDA Modernization Act excluded the small—well, it excluded drug compounders, for the most part; is that correct?

Ms. HAMBURG. That is correct. If a pharmacy was operating in accordance with certain conditions, then they were excluded.

Ms. DEGETTE. So the FDA didn't have authority over those types of compounders, correct?

Ms. HAMBURG. That is correct.

Ms. DEGETTE. So after the 1997 act was passed, when the FDA received complaints about drug compounding, it had to go over the hurdle of determining whether those conditions had been met or not before the FDA was determined to even have authority; is that correct?

Ms. HAMBURG. Correct.

Ms. DEGETTE. So what happened here is that the FDA was contacted in 2002 about some problems. They went into NECC, they found some problems, and there was a whole series of investigative efforts after that, correct?

Ms. HAMBURG. Yes.

Ms. DEGETTE. And one of the issues in this case and in other cases was whether the FDA even had authority to be investigating complaints, whether or not this particular manufacturer fell under the appropriate criteria, right?

Ms. HAMBURG. With respect to the public health threat that was identified in 2002, we went in and aggressively investigated and worked with the State of Massachusetts to get those contaminated products recalled to prevent ongoing damage to patients. Then, because this was a compounding pharmacy, with the primary responsibility for oversight resting with the Massachusetts State Board of Pharmacy, they were responsible for the efforts——

Ms. DEGETTE. "They"? Who is "they"?

Ms. HAMBURG. The Massachusetts State Board of Pharmacy.

Ms. DEGETTE. Massachusetts was primarily responsible because it was a compounding pharmacy, right?

Ms. HAMBURG. Because it was a compounding pharmacy.

Ms. DEGETTE. OK. So, in other cases, not particularly NECC but in other cases, when the FDA tried to assert jurisdiction over compounding pharmacies in similar situations, they were actually sued in court, the FDA was sued in court by these companies, saying the FDA didn't have jurisdiction over these pharmacies, correct?

Ms. HAMBURG. That is correct.

Ms. DEGETTE. And, in fact, there is a court case that covers part of the whole country that says the FDA doesn't have jurisdiction; is that right?

Ms. HAMBURG. The challenge we have today is that there is a patchwork of legal authorities that really oversee the regulatory actions that we can take. We have a split circuit court decision. There is a map that we have that shows that, you know, unfortunately, we have unclear, fragmented legal regulatory frameworks that make it very hard to understand how best to exercise enforcement.

Ms. DEGETTE. Well, and so if you have an emergency like this, if you have an emergency like this, sometimes what you are afraid of is—you are going to act aggressively, but you are afraid that you are going to be hauled into court. And that is why oftentimes you go to the State regulatory agency; is that correct?

Ms. HAMBURG. Absolutely. The fact that we have unclear, limited, and contested authorities and ambiguities in the law and a crazy quilt of legal authority has required us to be very reactive, responding to those serious public health threats, and selective. And, of course, every effort is resource-intensive, as you say, and often will end up in litigation.

Ms. DEGETTE. OK, so let me ask you this: If Congress clarified what we meant in the 1997 act with these large compounding pharmacies, that we, yes, indeed, intend to give the FDA jurisdiction, that will help you be able to protect these patients better by either doing inspections to prevent these problems in the first place or by requiring quick recalls; is that correct?

Ms. HAMBURG. Absolutely.

Ms. DEGETTE. Thank you.

Ms. HAMBURG. We clearly need additional authority.

Ms. DEGETTE. I just want to ask a really quick question of Dr. Smith.

I really appreciate the efforts that you are making since you took over. But, again, most of these things that happened—in fact, all of these things that happened—happened before your tenure, Dr. Smith.

And I guess I would like to know—and in reading all the documents and all of the history of this, it is obvious to me that the ball was dropped, and dropped in a big way, by the Massachusetts regulators. And so my question is, what is Massachusetts doing now to make sure this never happens again?

Ms. SMITH. Well, I agree with you that there were certainly missed opportunities and lapses of judgment that demonstrate significant irresponsibility. And we have taken action with the staff that demonstrated that.

In terms of what we are doing now, I think the highlight would be the enactment of the emergency regulations, importantly, which would require sterile compounding pharmacies to produce information regarding volume and distribution—the volume issue being so important because if you are making numerous batches, thousands of vials of material, then effectively you are acting more like a manufacturer than the more traditional compounder.

We also require pharmacies to provide information on any State or Federal investigations that concern them. That would allow us to have known that your State's board of pharmacy had, in fact, issued a cease-and-desist to NECC in April of 2011 for this same issue of providing bulk prescriptions that were not patient-specific.

And, lastly, we have done the—convening a special commission to really understand what are the best practices in strengthening the oversight of this evolving industry.

We clearly are committed to making sure that this doesn't happen again, and we want to do everything in our power to do that.

Ms. DEGETTE. Thank you.

Thank you very much, Mr. Chairman. I appreciate your indulgence.

Mr. STEARNS. The chairman of the full committee, Mr. Upton, the gentleman from Michigan.

Mr. UPTON. Thank you, Mr. Chairman.

I just want to remind all of us here that this committee has a very long tradition, even before John Dingell, of working with strong members to identify problems in this country, to expose that, and then coming back with legislation to fix it so it doesn't happen again.

And one of those, as we all review this case and see what was there—the recent inspection, the visible black particulate, the tacky mats, the leaking boiler, the bird flying around—I mean, it is just, what gives? I mean, if this was found just recently—and it is our understanding that there were similar types of contamination in earlier years—what is the problem without—what is the problem by not shutting down something like this until it is corrected?

And if you don't have the authority, then we need to make sure that it is there. And it seems pretty reasonable to me that, in fact, you did have the authority to not only have unannounced inspections but to come in and correct it so that it didn't get to this stage.

Certainly, with the deaths of people across the country and the questions that are raised today, as part of the tradition of this committee, we have to have the right information to find out if something is off track or whatever.

And I guess one of the concerns that I have is that, in a bipartisan letter that was sent nearly a month ago, we asked the FDA for documents, for internal communications, to find out what discussions were going on, what was the feedback from the company. And it is my understanding that to date we have some emails that have come back but not anywhere close to what we ought to have as we really try to move an investigation forward and try to get to the very bottom of this and make sure that it never can happen again.

And I would ask Commissioner Hamburg if we can have a commitment from you, as it relates back to the letter that we sent on October 17th, that we get the full cooperation from your staff so that we can come back and ask questions and really try to get to the bottom of this to identify where are the problems. Because, clearly, they were there, right?

Ms. HAMBURG. We will work very hard with you. We appreciate the work this committee is undertaking. We have tried to get you documents in a timely way. We have, you know, so far been able to get you——

Mr. UPTON. Not very many.

Ms. HAMBURG [continuing]. You know, the 2,000 pages of documents. But, unfortunately, we are also pursuing the active public

health investigation response, and many of the same people that are involved, have the right expertise and knowledge of the issues, are working on that at the same time that we are trying to get you that information.

And of course, as Congresswoman DeGette pointed out, this concerns activities, some of it going back many years to a different administration and different employees at the FDA. So we are going through, trying to get all those documents, and we will be continuing to provide you with the information you have requested.

Mr. UPTON. Well, I just want to say, I had a long discussion last month during the break with my colleague from Michigan, Mr. Dingell. Very frustrated about what was going on. Wanting to get to the bottom of this, wanting to make—you know, as we all think about the FDA's proper role, I mean, this would be it. I mean, as we all identify facilities in our own districts—I know that when I go visit, it is clean as a whistle. It really is. The people are proud to have the jobs that they have. It is as sterile as you can imagine.

And I can't, you know, for the life of me, as we read about this information from eyewitness accounts and inspections that were there before, and to have it go on and on and on without a follow-up, without—I mean, that is not—that is not what anyone is expecting the FDA to do. When you find this stuff, it needs to stop.

And, as Americans, we demand that for manufacturing here. We also expect it to happen overseas. And your inspections in China and other places, that the products that are being produced are safe, not only for Americans but all humans. And when we—you know, we get terribly frustrated.

I know you tried to call me yesterday afternoon. It was my first day back. And we are going to continue to communicate, I can assure you.

But we want to get to the bottom of this. We want to find out what really did break down and where are the questions that have to be answered so that, in fact, you do have the baseball bat to go after these companies that are—it is not right. And this is not going to be the last hearing, because we don't have the information that we need to proceed.

So I would like to get just—I know my time is expiring, but we would like to get a commitment from you that, in fact, you will be totally responsive to the questions that are asked by Republicans and Democrats so that we can figure out where this train got off the track so that we can put it on and we can assure every person in this country that, in fact, the FDA is working as it should.

And we shouldn't have to hear the stories that we did earlier this morning with Mrs. Lovelace and our constituents, whatever State that they are in. And I would like to get that from you and just assure you that we are not—this is not a one-time deal. We are going to get to the bottom of it.

Ms. HAMBURG. You have my absolute commitment that we will continue to work with you and all of your requests for additional information.

You have also touched on a very important point that I want to underscore, though, which is that we have responsibilities for oversight of manufacturers and drug facilities in this country and around the world, but our authorities to provide oversight of drug

manufacturers is very different than our authority to oversee compounding pharmacies, which are, in fact, exempted from important aspects of FDA law.

And there is, you know, this disconnect between different legal requirements in different parts of the country, as well. We have ambiguous, fragmented, unclear, and contested authorities in this particular realm of pharmacy and drug manufacturing practice.

And that is what our opportunity is now and what our responsibility, I think, is, to work together to really create new legislative authority that defines the best approaches, that gives us the broader authorities that we need to address this growing arena of what we call "nontraditional compounding" that involves larger volume, more complex products, including sterile products, and broader distribution, potentially putting more patients at risk.

And there are gaps in the oversight authorities of the States, who have primary responsibility for overseeing compounding pharmacies, and the FDA. And we need to make sure that we have a seamless system that protects patients.

Mr. STEARNS. The gentleman from California, Mr. Waxman, is recognized for 5 minutes.

Mr. WAXMAN. Thank you, Mr. Chairman.

I want to commend Chairman Upton for his statements and his questions because I think this committee needs to respond on a bipartisan basis.

And I think we need to correct the law, and we ought to try to do it before we leave at the end of this year for this simple reason: When you get into the next year, some of these interest groups are going to gear up to stop legislation. They will say that we really don't need to have the FDA look at these compounders. FDA regulates the manufacturers, but the compounders are going to be regulated at the State level.

Now, you are being criticized, Dr. Hamburg, as the head of the FDA, for the problems that were primarily the responsibility of the State of Massachusetts. And often we hear on this committee, "We ought to let the States handle things, not the Federal Government."

In fact, I want to express some sympathy for you at FDA because you are in a no-win situation. When the FDA asked for more data to determine whether a drug is safe and effective, or takes enforcement action for violations of good manufacturing practices, the agency is accused of being a job-killer, an over-regulator. But now when something terrible happens, we hear that something went wrong and everybody is quick to jump on you for not doing enough.

Now, if we expect you to do more, we better be sure that the statutory law gives you enough authority to do your job, if we want you to do the job and not the State to do the job.

And let me be very critical of the State. The State of Massachusetts dropped the ball. They entered into a consent decree with the company and said—it was a weaker consent decree than they originally started with, and said, oh, you ought to get an independent inspector. So the company hired an independent inspector. And then the independent inspector came back and said, everything is fine. And then there were questions about whether this was really an inspector that was independent, which is a good thing to keep

in mind when we say, let the companies decide who to pick to investigate themselves.

So let's look at what we can do now. How many compounding pharmacies are there in the United States?

Ms. HAMBURG. You know, we don't know the exact number because they are not required to register, and so, you know, we are really uncertain. But there are thousands of pharmacies that do compounding. We think that there are about 7,500 pharmacies that do more so-called advanced compounding and about 3,000 facilities that are doing sterile compounding.

Mr. WAXMAN. Now, compare that to manufacturers where there is no question that you have the jurisdiction to inspect them and to approve their drugs and to recall their drugs. How many manufacturers are there—manufacturing facilities compared to the compounding facilities?

Ms. HAMBURG. You know, there are about 5,600 manufacturers that we provide oversight for, including regular inspections. And there is a broader array of facilities that we also oversee in that context.

Mr. WAXMAN. Well, in 1997 Congress attempted to codify an FDA regulatory system with respect to these compounding pharmacies, but then the Supreme Court later invalidated a part of that law, raising the question of whether the rest of the law is still in force.

Some have argued the FDA still has the ability to cobble together other authorities to act to prevent this tragedy caused by NECC. I don't know if that was a realistic possibility or not. What I do know is that, at the very least, there is a dangerous lack of clarity in FDA's authority here, and we should fix that.

Do you think there is a lack of clarity?

Ms. HAMBURG. I think there is an enormous lack of clarity, and I think we should seize this opportunity to address it. We——

Mr. WAXMAN. What authority and enforcement tools does the FDA need to better enable you at the FDA to take effective action when you discover problems at compounding pharmacies?

Ms. HAMBURG. Well, we feel that there needs to be a risk-based framework that enables us to play our critical role in overseeing drugs that are going to the American people. Compounding has an important role in addressing medical needs, and traditional compounding is probably best overseen at the level of the State, though it should always be undertaken by a licensed pharmacist or physician and in accordance with a prescription for a patient for a specific medical need.

Mr. WAXMAN. We——

Ms. HAMBURG. But there is this area of nontraditional compounding, where we think really there needs to be focused attention and new legislation.

Mr. WAXMAN. Now, all pharmaceuticals that are compounded don't need to be regulated by the FDA, because the traditional way we think of it is a pharmacist putting together a prescription for somebody who has a special need. But now we have an example of a company that is shipping it all over the country. They are making a drug and they are shipping—they are like a manufacturer of the drug.

What we need from you is very specific authorities that you must have to be able to deal with this. And the second thing we need to recognize is your budget. Because if we give you authority and there are thousands of compounding pharmacies, your agency I can't imagine has the resources to regulate every single one of them, and we need to—you need to rely on the States to complement the FDA's oversight. Is that a fair statement, that you rely on the States?

Ms. HAMBURG. That is a fair statement.

And with respect to the authorities, I did outline in the testimony. But we clearly believe that for nontraditional compounders there should be Federal standards that would establish basic safety measures, including sterility controls. Could be enforced by the State or by the FDA, but those need to exist.

Then we need standards, new authorities around registration, so we know who is out there and what they are making. We need to be able to review records——

Mr. WAXMAN. Let me—you are absolutely right.

And I want to say to Chairman Upton and, for the record, all the members of this committee that we need to get this information. We have to get the right balance. We ought to do it before we leave at the end of the year and make it very clear that we are not just saying, "You are at fault, you are at fault, somebody else is at fault." We are going to be held responsible, as Members of Congress, to make sure the law is clear and that the agency has the ability and resources to do the job that everybody expects you should have done. And we want to make sure that you are able to do it.

Thank you, Mr. Chairman.

Mr. STEARNS. The gentleman's time has expired.

The gentleman from Texas is recognized for 5 minutes.

Mr. BARTON. Thank you, Mr. Chairman.

I mean, we have a tragedy of significant proportions here. Thirty-two people have died; probably more will. We have a bipartisan investigation before this subcommittee. And we understand that, you know, business as usual is not acceptable.

Having said that, apparently the FDA has decided this is something that they can use to be able to get more authority to regulate or inspect certain transactions that compounding pharmacies do. If there really is a lack of regulatory authority at some level, then that is a legitimate policy recommendation. But if there is not a lack of regulatory authority in existence in State and Federal law right now, then it is unnecessary.

And my first question is to both Dr. Hamburg and Dr. Smith. Are you all both stating that under current State and Federal law neither the State nor the FDA had the authority to seize these drugs or to shut this company down?

Ms. HAMBURG. I think it is important to understand——

Mr. BARTON. I want a—I don't need a long—I think it is important. If the State of Massachusetts doesn't have the authority and the FDA doesn't have the authority, that is one thing. But we have a warning letter, 2006, issued by the FDA. Now, this is before you were the Commissioner. It says, "Failure to promptly correct these deviations may result in additional regulatory action without fur-

ther notice, including seizure or injunction against you and your firm." So, in 2006, in the FDA's warning letter, it was the thought at that time that the FDA had sufficient authority.

And Dr. Smith, on behalf of the Massachusetts—she has only been on the job 3 weeks, so we can't hold her liable for what happened, you know, 10 years ago, 6 years ago, 7 years ago. But I don't think there is any question that if Massachusetts felt there was a violation, they had the authority to shut it down.

So, you know, I think we ought to work on using the authority that we have, as opposed to trying to get additional authority at the Federal level.

The FDA went in and inspected this particular company on at least two different occasions and, as far as I can tell, other than issuing one warning letter, didn't do anything at all.

Ms. HAMBURG. The truth is that in the initial inspections, we worked very closely with the Massachusetts Board of Pharmacy, which has the responsibility for licensure and oversight on a day-to-day basis of compounding pharmacies, but——

Mr. BARTON. So, again, go back and answer my question.

Ms. HAMBURG [continuing]. We acted to make sure that the contaminated product was recalled and not continuing to put people at risk. Our first priority was——

Mr. BARTON. So you are saying the FDA did have the authority or did not have the authority?

Ms. HAMBURG. We worked closely with Massachusetts, who had——

Mr. BARTON. Can you ever give a straight answer to the question?

Ms. HAMBURG [continuing]. The primary responsibility for the oversight of that facility.

Mr. BARTON. Either you do or you don't.

Ms. HAMBURG. I think, you know, what is very clear is that——

Mr. BARTON. What is very clear is that you don't want to answer the question.

Ms. HAMBURG. No, it is complicated, and that is reflected here.

But the responsibilities are different. What FDA has clear and strong responsibility for and oversight of——

Mr. BARTON. Let me ask Dr. Smith.

Ms. HAMBURG [continuing]. Is drug manufacturers.

Mr. BARTON. Dr. Smith, does your State——

Ms. HAMBURG. These are held to a different standard. Compounding pharmacies are——

Mr. BARTON. Does your State agency have the authority to shut this company down if you see a clear violation of the law, yes or no?

Ms. SMITH. Yes, it does.

Mr. BARTON. OK.

Ms. SMITH. And, in fact, we——

Mr. BARTON. Thank you. Now, if you——

Ms. HAMBURG. But the State of Massachusetts——

Mr. BARTON. At least you got——

Ms. HAMBURG [continuing]. Has the oversight responsibility for compounding pharmacies on a day-to-day basis. FDA has a different set of authorities.

And the challenge is that these authorities, as evidenced by that map, are fragmented. And what enforcement actions we can take have to be seen through different lenses in different parts of the country.

Mr. BARTON. All right.

Ms. HAMBURG. We don't have clear——

Mr. BARTON. I am going to try one more time, Dr. Hamburg. Under current law, does the Food and Drug Administration of the United States of America have authority over adulterated drugs?

Ms. HAMBURG. We have authority over adulterated drugs, and——

Mr. BARTON. Thank you.

Ms. HAMBURG [continuing]. We can take actions in relation to that.

Mr. BARTON. OK.

Mr. DINGELL. May the Congressman from Texas have 1 additional minute? And I would ask that he would yield to me.

Mr. STEARNS. By unanimous consent, so ordered.

Mr. BARTON. And I would be happy to yield to my good friend, the gentleman from Michigan.

Mr. DINGELL. I thank my friend.

Commissioner, two agencies here have dropped the ball. The Massachusetts agency has had to fire its head because it didn't do its job. Your agency—and I don't want you to be defensive; I just want you to recognize a hard fact. Your agency did not use your power to define who is a manufacturer. Here you have an agency that is—that in just one has sold over 17,000 doses in something like 23 States.

Don't you have the authority to define who is a manufacturer and who is a compounder? And if you do, why didn't you do it?

Ms. HAMBURG. The problem is that the current legal regulatory framework says either you are a compounder or you are a manufacturer, and there, in fact, is——

Mr. DINGELL. And you may define both, may you not? You have that authority, and you did not do it.

Ms. HAMBURG. I——

Mr. DINGELL. And I thank the gentleman for yielding.

Ms. HAMBURG. The concern, though, is that if it is all or nothing that way, then these facilities, if they were defined as manufacturers——

Mr. DINGELL. Commissioner, we are trying to solve the problem. This is not an issue of where you are here to defend yourself. If you choose to do that, you are going to have a very hard time in this committee. We do not tolerate that kind of foolishness, and I would assure you that you are putting your head in the noose.

I would urge you to just cooperate with us and with my good friend and give us the answers that we need——

Mr. BARTON. All right. Now——

Mr. DINGELL [continuing]. So that you can address your problems——

Mr. BARTON [continuing]. If I can reclaim the time I no longer have——

Mr. STEARNS. Just to recognize where we are, we had a unanimous consent to give Mr. Dingell 1 minute, and the time now belongs to Mr. Barton.

Mr. BARTON. I am just going to——

Mr. STEARNS. If you would finish up and we will move on to——

Mr. BARTON. Yes, I will be quick.

I want to be explicitly clear. If there really is a regulatory gap—based on the record that I have reviewed, I don't believe there is. But if there is, I suggest there is a bipartisan coalition on this subcommittee and full committee that will move legislation to correct it.

If, however, there is no regulatory gap, I also think there is a bipartisan coalition on this subcommittee and full committee to work to make sure that the State and the Federal agencies with jurisdiction work together to solve this problem and to prevent it from happening in the future.

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

Mr. STEARNS. Yield back.

And I want to thank the dean of the House of Representatives for his taking the initiative to really get the Commissioner to answer the question that both Mr. Barton and myself and others have asked, is whether you have the jurisdiction, and I think the answer is yes.

Ms. HAMBURG. No——

Mr. STEARNS. We recognize for 5 minutes Mr. Dingell.

Mr. DINGELL. I thank you, Mr. Chairman.

Commissioner, I would appreciate "yes" or "no" answers here.

Do you have sufficient authority to inspect compounding pharmacies, yes or no?

Ms. HAMBURG. No.

Mr. DINGELL. Would you please submit is to us what authorities you need so that we can see to it that it is done?

Do you have the authority to access all records when inspecting a compounding pharmacy, yes or no?

Ms. HAMBURG. No.

Mr. DINGELL. Please submit to us the information on what you need so we can see to it that that is given to you.

Do you have authority to require compounding authorities to—rather, compounding pharmacies to register with FDA, yes or no?

Ms. HAMBURG. No.

Mr. DINGELL. Would you please submit to us the authorities that are needed so that we can address that problem?

All right. Do you have the authority to require compounding pharmacies to report adverse events to FDA, yes or no?

Ms. HAMBURG. No.

Mr. STEARNS. Would you please submit to us what authorities you need in that area?

You heard earlier my question about whether or not you have the authority to define who is a compounding pharmacy and who is a manufacturer. Do you have authority to do that or not, yes or no?

Ms. HAMBURG. Yes, on a very technical level.

Mr. DINGELL. All right. If you need some reform of that authority, please submit that information to us.

Ms. HAMBURG. We definitely do.

Mr. DINGELL. Commissioner, do you have authority to require compounding pharmacies to follow good compounding or something equivalent to good manufacturing practices, yes or no?

Ms. HAMBURG. No, we do not.

Mr. DINGELL. Would you please submit to us the authority that you require?

Now, this question to both you and to Dr. Smith: Do you have sufficient authority between your agencies, State agencies and the Federal agencies, to assure that you are able to coordinate your authorities and to achieve the necessary controls over both manufacturers and compounding pharmacies?

Ms. HAMBURG. I believe we do not.

Mr. DINGELL. You do not.

What is your view on that, Dr. Smith? Yes or no?

Ms. SMITH. We don't regulate or oversee manufacturing, so——

Mr. DINGELL. OK, but can you define a compounding pharmacy so that you can define your authority? We have here something where a major problem fell between the cracks. Please submit the answer to us for the purposes of the record.

Now, again, to the Commissioner, do you have authority to require compounding pharmacies to indicate on the label of their product that the product was compounded and not approved by FDA, yes or no?

Ms. HAMBURG. We do not.

Mr. DINGELL. Would you please submit the authority—the authority that you need?

Commissioner, it does not sound to me like FDA has authorities to oversee compounding pharmacies, and there is a question of your authority to define who is a compounding pharmacy. Do you have efficient—do you have sufficient authority to oversee compounding pharmacies now, yes or no?

Ms. HAMBURG. We do not, no.

Mr. DINGELL. OK. Please submit to us your suggestions for that authority to be given.

Do you—would you submit to the committee any additional authorities that I have not been able to define here this morning that we should address to you?

Now, Commissioner Hamburg, your agency is in receipt of two letters dated October 9 and 16, 2012, from my office regarding this situation. When will you submit to us a response to those letters so that we can have that information available to us as the committee proceeds?

Ms. HAMBURG. We will get you those responses as soon as possible.

Mr. DINGELL. As soon as you can.

Mr. Chairman, with thanks, I return to you 24 minutes.

Mr. STEARNS. I think——

Mr. DINGELL. One more question, Mr. Chairman. Those two letters, I would ask that they be inserted in the record and the response that will be received by the committee.

Mr. STEARNS. We have seen those letters. By unanimous consent, so ordered.

Mr. DINGELL. Thank you.

Mr. STEARNS. And I thank the gentleman from Michigan.

The gentleman from Nebraska, Mr. Terry, is recognized for 5 minutes.

Mr. TERRY. Thank you, Mr. Chairman.

Here—I want to follow through on some of the gentleman from Michigan, Mr. Dingell's questions because I really do think that is at the heart of us trying to figure out where our jurisdiction lies or doesn't lie with the FDA and our role.

So I have toured compounding facilities in my district, which usually are small operations. In the part of a current pharmacy, somebody brings in a prescription that is unique, they compound it, and it is for that patient. That is compounding.

And I don't think the FDA would want—and that is a question for a different day—the jurisdiction to go into every pharmacy that has compounding abilities to make something specific for one of their clients. And that is why that has been reserved, I assume, in those discussions, the gentlelady from Colorado, of why it was put in the States' hands that are best able to do that.

So now when we focus on the New England Compounding Center, it may have called itself "compounding center," but it was a large manufacturing. We know that through its past violations that have come to the attention of both the State pharmacy board and the FDA in the past. So we then have a 2011 incident in Denver where pallets of a drug was found; a Colorado board of pharmacies issues a cease and desist. So now what we have is mass manufacturing of a specific drug for nonspecific people. To me, that is the definition of "manufacturing."

So, Ms. Honorable Hamburg, is the issue, then, that the definition of "manufacturing" within that bill isn't clear enough for the FDA? Because it seems pretty clear, if you are mass producing, you are sending it into interstate commerce and it is not for a specific patient, that that is not compounding, that is manufacturing.

Ms. HAMBURG. I think that this has been an evolving industry and that we do have a problem that existing law and authority is——

Mr. TERRY. What specifically——

Ms. HAMBURG. It is on or off——

Mr. TERRY. Let me interrupt you, since you talk over us.

I am looking for the specifics in the law that say that there is lack of clarity on the definition of "manufacturing." Because that seems to be the hook that you are putting your hat on. Can you specify in the act that we have to tighten the definitions?

Ms. HAMBURG. Currently, as we have discussed, there is huge disagreement about the FDA authorities, and the courts have split on the interpretation of authorities for compounding——

Mr. TERRY. Will you define the parts of the statute that we need to focus on regarding tightening the definition of "manufacturing"?

Ms. HAMBURG. The problem is that, with this evolving industry, there is a gray area. If we would be to regulate the thousands of compounders——

Mr. TERRY. That is a great speech. Can you refer me to the part of the statute that we need to focus on, yes or no?

Ms. HAMBURG. I am sorry, could you repeat——

Mr. TERRY. Refer me to the appropriate part of the statute that lacks the clarity of which you complain.

Ms. HAMBURG. The FDA has the authority to act against——

Mr. TERRY. Manufacturers.

Ms. HAMBURG [continuing]. Manufacturers.

Mr. TERRY. And this is generally manufacturers——

Ms. HAMBURG. We have the oversight of drug manufacturers, and with that comes a set of activities——

Mr. TERRY. All right.

Ms. HAMBURG [continuing]. That do not apply to compounders, including the——

Mr. TERRY. So you will not refer me to a specific section of which you feel lacks clarity.

One last question for Dr. Smith.

This is very frustrating, madam.

Dr. Smith, you are in a really tough place, and you have done a great job. You have presented well today. But I am very curious. With all of the knowledge that was brought to the State board—a colossal failure here. You said you are looking into that and putting the pieces together. I am just curious, is there any evidence of a special relationship between the State board and this manufacturer? Because it seems like somebody is covering for somebody.

Ms. SMITH. Well, we are as concerned about the missed opportunities as you are. And there are numerous, numerous episodes of that. We are in the process, as I said, of reviewing just that through interviews and through the exhaustive document reviews that we are doing and reviewing the documents that we have produced for this committee. It is, you know, thousands and thousands of pages.

So I can't—I don't know the answer to your question, but we are trying to——

Mr. TERRY. Well, I appreciate that you are looking into that.

Just the last 5 seconds, Madam Honorable Hamburg. Getting your testimony at 1:30 a.m., most of us are sleeping then, so I guess the whole purpose was to not let us see in advance your testimony.

I yield back.

Mr. STEARNS. The gentleman yields back.

The gentleman from Massachusetts, Mr. Markey, is recognized for 5 minutes.

Mr. MARKEY. Thank you, Mr. Chairman.

Ms. Hamburg, I have introduced legislation to give the FDA authority to define which compounding pharmacies should be required to register as manufacturers. Would you support that?

Ms. HAMBURG. We think it is very important that we have additional legislation in this area and that compounders, in fact, register and that it can be defined, what they are doing, what they are manufacturing, and what the appropriate regulatory oversight would be.

Mr. MARKEY. I have introduced legislation to give the FDA authority to require compounding pharmacies to compound safe drugs using safe practices. Would you support that?

Ms. HAMBURG. I do support that.

Mr. MARKEY. I have introduced legislation to give FDA authority to conduct the same inspections and request the same documents as it can from manufacturers. Do you support that?

Ms. HAMBURG. It is enormously important that we have the authority to go in and be able to do full inspections and review documents, collect samples, et cetera.

Mr. MARKEY. I have introduced legislation that requires compounding pharmacies to submit reports of adverse reactions or safety problems to the FDA. Do you support the FDA having that authority?

Ms. HAMBURG. Yes. It is currently a gap, that adverse events are not required to be reported from compounding pharmacies.

Mr. MARKEY. And I have introduced legislation to require compounded drugs to be labeled. Do you believe that that authority should be given to you?

Ms. HAMBURG. Yes, we do.

Mr. MARKEY. And I might say, the legislation also allows traditional compounding pharmacies, those which are just doing individual doses to individual patients, to continue to stay under State jurisdiction. Do you agree with that?

Ms. HAMBURG. Traditional compounding, one patient, one prescription——

Mr. MARKEY. Yes.

Ms. HAMBURG [continuing]. Should be overseen by a licensed physician or pharmacist, but it does not require the FDA oversight.

It is this nontraditional compounding area where the volume is larger, the distribution is larger, the products are more complex, where we think we lack the authorities that we need. And we appreciate that you are introducing legislation, and we will work actively with you——

Mr. MARKEY. Thank you.

Ms. HAMBURG [continuing]. In order to an achieve the important goal.

Mr. MARKEY. I think it is critical, given today's hearing, given what we have heard from the witnesses, the pain that it has caused, the regulatory black hole that obviously has to be closed, that we pass legislation that gives you these authorities——

Ms. HAMBURG. I agree with you.

Mr. MARKEY [continuing]. So that children will have to look to the history books to find that there ever was such a catastrophe as is being suffered by hundreds of families across the country right now. And so I just hope that we can move quickly on legislation to give you that authority because I think you are the cop on the beat and we have to make sure that you have the authority which you need in order to enforce the law.

And, Dr. Smith, I want to commend you and Governor Patrick for the decisive manner in which you have responded to this tragedy. You have undertaken an aggressive investigation and held the companies involved and some members of your staff accountable and put in place stringent emergency regulations for compounding pharmacies in Massachusetts.

We have learned that this tragedy was enabled by a regulatory black hole that allowed a drug manufacturer, NECC, to masquerade as a pharmacy, producing massive amounts, quantities of

drugs with little or no Federal oversight, and able to sell these vials all across the country to dozens of States without full Federal regulation.

And there were complaints that had been reported as long as 10 years ago. Starting in 1999 with the first complaint, State regulators repeatedly failed to take strong action, such as withdrawing NECC's license in 2006. The State even waived the company's proposed probation as long as it got a clean bill of health from an independent evaluator. But when that same independent evaluator was convicted of selling unsafe medical sterilization equipment that blinded 18 patients, Massachusetts did nothing to make sure the clean bill of health that the New England Compounding Center had received was reexamined.

Dr. Smith, have you been able to determine why those decisions were made back then through interviews with the staff that were there at that time?

Ms. SMITH. No, we have not. We have done interviews, as you allude to, and we have not been able to really understand why they made those decisions. In retrospect, clearly there were missed opportunities for the Board of Pharmacy, as you point out, in 2006 to take decisive action, and it did not. And we are trying to understand that, but we don't at this point.

Mr. MARKEY. Are all of those individuals' emails and other documents from that period available for review?

Ms. SMITH. Yes. We have—we produced for this committee thousands of—thousands of pages of emails. And those are all being reviewed.

Mr. MARKEY. Is it possible that some of those emails and documents have been destroyed in the period of time from 2006 and prior to today?

Ms. SMITH. Well, I am not—I wouldn't be sure of that. I can tell you that the numbers of emails from the earlier, prior years are far fewer than what we have been able to obtain more recently.

Mr. MARKEY. So Massachusetts is, in the very near future, going to have the strongest compounding pharmacy regulation in the country. But that does not protect us, does it, from other States having weak laws, which could then sell compounded drugs into Massachusetts——

Ms. SMITH. That is correct.

Mr. MARKEY [continuing]. Or the other 49 States?

So you just heard the list of powers which I asked Dr. Hamburg if she would support being given to the FDA. Do you support giving the FDA those same powers so that they can be the national cop on the beat to protect against one State becoming the place where a rogue compounder then terrorizes and harms the rest of the country?

Ms. SMITH. Absolutely.

Mr. MARKEY. I thank you. I thank all of you for your service.

And I thank you, Mr. Chairman.

Mr. STEARNS. I thank the gentleman and recognize Dr. Burgess for 5 minutes.

Mr. BURGESS. I thank the chair for the recognition.

Dr. Hamburg, again, thank you for being here today.

Let me ask you, you made a statement a minute ago in response to another Member's question that you favored a risk-based system; is that correct?

Ms. HAMBURG. We do favor a risk-based——

Mr. BURGESS. Let me just stop you for a second, because, I mean, this country was—company was bad news from the day it started back in the '90s. They, as is my understanding from looking at the materials provided to us, they shipped preprinted prescription forms to various clinics around the country in clear violation of what they should be doing.

And then you have—the FDA, not you, but the FDA has assembled a 10- or 15-year history of repeated violations and areas where this company has shown itself to be unsafe. So if you want to have a risk-based system, this company is too risky. You can't risk it. Don't do a risk-based system for this company. It is through. And, in all honesty, it should have been terminated by the FDA, multiple branch points along the way—2002, 2004, 2006, 2008. We see the documents. It should have happened.

Now, I guess, listening to your testimony today, I must be given to believe that what you have been doing is collecting the data set so that what Congress finally passed a law to allow you to prevent this from happening you would then prevent it. Is that what I am understanding? That you lack complete and total authority to do anything at all even though you saw this stuff happening?

Ms. HAMBURG. You know, we worked very hard when the first problems at NECC were identified with the State to address them aggressively. But our authorities around compounding pharmacies are unclear, limited——

Mr. BURGESS. Yes, let me stop you.

Ms. HAMBURG [continuing]. And untested.

Mr. BURGESS. We have been down this road before——

Ms. HAMBURG. We need——

Mr. BURGESS [continuing]. And we are not buying it. We are just not buying it, Dr. Hamburg, in all honesty.

You have an evidence binder in front of you. Tab 15, look at it, if you will. It is a letter dated October 31st, 2008. We have heard other people reference a 2006 letter where the FDA, the FDA, in writing to this compounding pharmacy, say, "Failure to do so may result in an enforcement action, including a seizure of the firm's products and/or an injunction against the firm and its principals." That is pretty strong language.

Now, you lacked the authority to do anything and yet you sent a letter like this? Was this letter sent in error? You really didn't have that authority, and it was an empty threat; is that what I am to understand?

Ms. HAMBURG. As, you know, was pointed out, I was not present at the FDA at the time, and I cannot speak to all of the issues. But there—clearly, there was an effort to assert authority——

Mr. BURGESS. Well, let me just ask you——

Ms. HAMBURG [continuing]. Around an issue that was very different than the issue about sterile compounds——

Mr. BURGESS. OK. But this letter was issued in error; is that what I am to understand? It was an error, that the FDA sent this,

even though it was a previous administration, a previous Commissioner?

Ms. HAMBURG. There were—in 2004, the FDA was asked to take a look at an issue that involved a specific product, Trypan Blue, and whether or not NECC was making it inappropriately.

Mr. BURGESS. OK. With all due respect here—and our time is limited. I don't mean to be rude, but we really have to pursue this.

Did you, did anyone at the FDA, previous Commissioner, previous administration, did anyone get a legal memo from your legal department saying, "Hey, you didn't have the authority to do that, so you better back off"? Is there such a memo in existence?

Ms. HAMBURG. There was a lot of internal discussion. The courts were split on what our authority——

Mr. BURGESS. So was there a memo delivered from the Commissioner?

Ms. HAMBURG. Well, at that time, there was ongoing litigation, and——

Mr. BURGESS. May we on the committee have access to those internal memos that said you didn't have the authority to write that letter?

Ms. HAMBURG. That isn't what I said, and I apologize if it came across that way. What I was saying was that an inspection was done in response to a specific complaint, and then, with respect to the actions taken, there was ambiguity in the law, ongoing litigation——

Mr. BURGESS. Yes, but there is no ambiguity.

Ms. HAMBURG [continuing]. Discussions within FDA, as I understand it, about——

Mr. BURGESS. OK, let me try it from another perspective, if I could.

Ms. HAMBURG [continuing]. What enforcement could be used to take action.

Mr. BURGESS. We all saw on television the company being raided, the computers being seized. Did you do that and you didn't have the authority to do that?

Ms. HAMBURG. In the—I mean, you are asking me about one specific question that had to do with the warning letter, which is a very discrete and different problem than what we are talking about——

Mr. BURGESS. But you assert an authority which you are now telling us you don't have in that letter. Now——

Ms. HAMBURG. I think you just need to look at the map and see that the authority that is used to oversee compounding pharmacies is very fragmented. We have different court decisions applying different legal regulatory frameworks to different parts of the country that cannot serve patients well.

We need to have a strengthened and clarified legal regulatory authority that gives us some of the additional authorities over——

Mr. BURGESS. OK. Once again, let me just ask you as straightforward and simply as I can, do you have the authority to regulate the manufacturer, or if a compound is—of the manufacturer of these compounds or if the drug is adulterated in some form? Do you have that authority, as it exists today?

Ms. HAMBURG. We have many more authorities over drug manufacturers than compounding pharmacies. And that limits our ability to effectively ensure the safety and quality——

Mr. STEARNS. Dr. Hamburg——

Mr. BURGESS. Well, again, let me just ask it in the simplest way that I can. How many companies are out there labeled as compounding pharmacies that ship 17,000 doses of sterile, preservative-free steroids every year?

Ms. HAMBURG. The problem is that compounding pharmacies are not required——

Mr. BURGESS. How many? The question is, how many?

Ms. HAMBURG [continuing]. To register with us. We don't know how many compounding pharmacies are, in fact, engaging in those kinds of practices.

What we do know is that the industry, though, has evolved and that there are an increasing number of nontraditional compounders who are acting, for example, with hospitals and clinics——

Mr. BURGESS. Look——

Ms. HAMBURG [continuing]. Are outsourcing to them——

Mr. BURGESS [continuing]. We heard testimony from the widow of a victim. And you could tell that there was some bitterness in her voice against the company—or, the clinic that had provided the steroid injections. "How could they buy it from someone if they weren't sure?"

But, you know, I am a doctor, you are a doctor, Dr. Smith, you are a physician. I mean, you take a vial off the shelf, you make some assumptions as to its potency and its sterility. In this country, we stipulate that, because you have done your job at the FDA, we don't have to come and ask additional questions before we administer that to a patient.

Now you are telling me that that is not the case and that the FDA lacks the authority to assert that the safety and effectiveness of those medicines that are coming off the shelf is, in fact, valid?

Ms. HAMBURG. We have the authority with drug manufacturers to oversee the safety, efficacy, and manufacturing quality.

Mr. BURGESS. Correct.

Ms. HAMBURG. We do not have——

Mr. BURGESS. And if you are making 17,000 doses of sterile, preservative-free, injectable steroids every year, you are a manufacturer. There is no other word for it.

Mr. STEARNS. The gentleman's time has expired.

Mr. BURGESS. I thank the gentleman.

Mr. STEARNS. Let the record show, Dr. Hamburg, he asked you a question. You are under oath. You have an obligation to answer "yes" or "no."

Ms. DEGETTE. She tried to answer——

Ms. HAMBURG. I was attempting to, and——

Mr. STEARNS. And let the record show——

Ms. HAMBURG [continuing]. I am sorry if I did not.

Mr. STEARNS [continuing]. That Dr. Burgess asked you a question time and time again, the same question, and you would not answer "yes" or "no."

Let me recognize——

Ms. HAMBURG. We do not have the authority over compounding authorities——

Mr. STEARNS. That is—Dr. Hamburg, we understand that.

Ms. HAMBURG [continuing]. That we have over drug manufacturers.

Ms. DEGETTE. Wait a minute.

Mr. STEARNS. The gentlelady from Florida, Ms. Castor, is recognized for 5 minutes.

Oh, Ms. Schakowsky. Oh, I am sorry. Yes, welcome.

Ms. SCHAKOWSKY. This is for Dr. Smith.

In the aftermath of this tragedy, we have learned some troubling facts about the Massachusetts Board of Registration and Pharmacy and how it dealt with NECC in the past. And it raises some questions about whether the board was too close to NECC and whether the board did enough to prevent conflicts of interest from affecting its decisions.

So I wanted to ask you, Dr. Smith, about Sophia Pasedis, one of the members of the board. I understand she is gone now; is that true?

Ms. SMITH. No. We have asked her to resign, but she declined.

Ms. SCHAKOWSKY. So how long has she served on the board?

Ms. SMITH. I don't have that in front of me, but it has been for several years. She was there in the previous administration.

Ms. SCHAKOWSKY. And what is her affiliation with NECC or its sister companies?

Ms. SMITH. She had previously worked for NECC. I am sorry—she started in the summer of 2004. She had previously worked for NECC and then subsequently went to Ameridose, a company that was also owned by Mr. Cadden.

Ms. SCHAKOWSKY. So I understand that she was actually vice president of regulatory affairs and compliance at Ameridose.

Ms. SMITH. Yes. And she is the pharmacy of record there.

Ms. SCHAKOWSKY. Did Ms. Pasedis adequately recuse herself from board actions related to these companies?

Ms. SMITH. In our review of the minutes of the board meetings, it is clear that on several occasions there is a specific indication that she did recuse herself. However, there are some minutes that don't—that are silent on the issue, don't say either way. And because of that, the fact that it was unclear she appropriately recused herself—although in interviews she declares that she did—because of the lack of clarity, we asked her to resign, which, as I said, she declined.

Ms. SCHAKOWSKY. So I am glad that you attempted to take action to remove her, but there is still a lot of questions about whether her role on the board during much of the time when Massachusetts was receiving complaints softened the actions of the board that the board was willing to take against NECC.

In 2004, after first identifying significant problems at NECC, the board proposed a tough consent agreement with real sanctions. But something happened in the interim, and the consent decree that was actually signed in 2006 was much weaker than in the initial proposal.

Do you know how this happened and why the board proposed weaker penalties even after they had received additional reports of problems at NECC?

Ms. SMITH. We don't know how that happened, and, as I mentioned, we are very interested and have been attempting to find that out. Our interviews with board members about that precise issue have been—have not yielded definitive information. Most simply state that they don't recall.

Ms. SCHAKOWSKY. So one of the problems with the 2006 consent agreement was that it required NECC to be independently audited but then let NECC have significant input into who its independent evaluator would be.

So, Dr. Smith, did NECC participate in the selection of PSI as its independent auditor—evaluator?

Ms. SMITH. Well, we are unsure. We have been reviewing the records to, in fact, try to determine who did make the final decision regarding who that independent evaluator should be. And it is unclear, from the documents that we have found, who did do that.

Ms. SCHAKOWSKY. And is it common for a party to help select its own evaluator?

Ms. SMITH. I can't speak to whether or not it was common. You could certainly imagine that that would be problematic. But we haven't been able to determine who, in fact, chose the evaluator.

Ms. SCHAKOWSKY. Is it still the practice?

Ms. SMITH. Well, it would be—currently, I am not aware of any current actions that are involving an outside evaluator. As we proceed, as I mentioned, we are really looking at both the best practices around other States for the Board of Pharmacy, and so that would be the kind of thing we would include.

Ms. SCHAKOWSKY. Well, let me just say, at the time that PSI was selected to act as an independent evaluator, one of its executives, Ross Caputo, was facing trial for defrauding the FDA and selling unapproved sterilization equipment to hospitals that caused blindness in patients. And he was later convicted.

So in 2006 your agency sent a letter to NECC telling them that they had "satisfactorily completed," unquote, the conditions of the consent agreement based on NECC's compliance with the follow-up actions identified in PSA's audit report of the company; is that correct?

Ms. SMITH. That is correct.

Ms. SCHAKOWSKY. So were any of the Massachusetts Board of Registration and Pharmacy staff aware of Mr. Caputo's Federal conviction when they found NECC had satisfactorily completed PSI's recommended actions?

Ms. SMITH. As far as we can tell through our interviews with staff and the board members, they were not made aware of the fact that the primary evaluator, Mr. Caputo, had, in fact, been convicted of those Federal crimes. The staff were aware, but, as I have mentioned, and shockingly so, they did not share that information with the board.

Ms. SCHAKOWSKY. Well, you know, we have turned up a number of problems, but, one, it seems that the NECC was too close to the board and its members, and it seems like the board was more in-

terested, maybe, in protecting pharmacists than in protecting consumers.

We have a lot of work to do, but it seems like that some of the solutions that we have laid out, at least on the Federal level for the FDA, are fairly clear. And I am hoping that at the State level, as well, that these problems will be—you will get to the root of them.

Thank you.

Mr. STEARNS. The gentlelady's time has expired.

The gentleman from Pennsylvania, Mr. Murphy, is recognized for 5 minutes.

Mr. MURPHY. Thank you.

Dr. Smith, in your testimony, you had stated that you have uncovered a number of problems where PSI executives and others did not provide information to people. You said you have found no evidence to indicate the executive directors or staff attorney of the board provided crucial information to the board, and yet the board had to vote on something without that information. Am I correct?

Ms. SMITH. That is right.

Mr. MURPHY. And you have given a number of other examples of a breakdown within the structure and have taken action toward people when you found that they were not properly informing or following the rules?

Ms. SMITH. That is correct.

Mr. MURPHY. OK. Is there anything also within the laws, as you understand it, that you have the authority within Massachusetts, are required, to pass information up to the FDA on any of these problems that occur?

Ms. SMITH. There is nothing in our practices or our regulations that I am aware of that requires that kind of information share.

Mr. MURPHY. Do you do it anyway?

Ms. SMITH. Certainly, since this investigation or this episode has begun, we have worked in partnership with the FDA and, in fact, have done all of the inspections together. That is an area, as I mentioned, when we move forward to determine what sorts of policies we should have about information sharing——

Mr. MURPHY. Thank you.

Ms. SMITH [continuing]. Whether it should be required as opposed to on a case-by-case basis.

Mr. MURPHY. It is helpful internally to identify those breakdowns, too.

Ms. Hamburg, is there someone at the FDA who routinely reviews State actions and communicates with them from your level down to the States when there are problems occurring? Is there anybody who reads or reviews anything with the States at all right now?

Ms. HAMBURG. There is not a system in statute——

Mr. MURPHY. But is there anybody who does that?

Ms. HAMBURG [continuing]. Or in practice where there is that kind of back-and-forth communication on a routine basis. When there is a serious problem, as occurred in this case, you know, we mobilize into action very quickly. We have——

Mr. MURPHY. Who is it that is mobilized in the FDA to then work with States?

Ms. HAMBURG. Different components of FDA, depending on the nature of the problem.

Mr. MURPHY. Is there a particular person?

Ms. HAMBURG. We have district offices, and they are sort of the first line in terms of identification of a problem——

Mr. MURPHY. I am just trying to get some specifics here.

Ms. HAMBURG [continuing]. And responding——

Mr. MURPHY. I am trying to lay out here that Dr. Smith did a thorough internal review and found a number of breakdowns that people weren't communicating with one another.

I am trying to find out within the FDA—regardless of regulations, obviously if someone with the FDA was talking to the States, someone has the authority to talk to States. And I am trying to find out if you have identified structural changes needed within the FDA to make sure you are communicating within FDA that information is coming to your desk for review. Have you made any of those changes or reviews?

Ms. HAMBURG. I think part of the issue here is there are not formalized systems. There certainly are opportunities to improve communication. But it also is a broader issue, that compounding pharmacies——

Mr. MURPHY. Hold on. Really, I am trying to help.

Ms. HAMBURG. Uh-huh.

Mr. MURPHY. And you are obfuscating.

Dr. Smith, very cogent leadership, says, if there are problems, identify the problems, we went after the problems. I am just trying to find out, do you even have—you don't have to wait for authority to find out within the FDA who can have the authority to review these things. Do you have it, yes or no?

Ms. HAMBURG. We—well, I am not sure what authority you mean.

Mr. MURPHY. Well, the authority to review if there are problems with the States and manufacturing, et cetera.

Ms. HAMBURG. We don't always get the reports is the issue. When we do get the reports, then we have our district offices and Office of Regulatory Affairs——

Mr. MURPHY. OK. Have you met with those people since from the district offices to review——

Ms. HAMBURG. Yes.

Mr. MURPHY. OK. Thank——

Ms. HAMBURG. We have been working very closely with them. And, you know, every day there are issues that involve our working with States——

Mr. MURPHY. Well, let me ask another area, too, in terms of identifying people. In terms of dealing with the definition of "compounding pharmacy" versus "manufacturer," who within the FDA is responsible for defining that?

Ms. HAMBURG. Well, the—it is not just in FDA. It is Congress——

Mr. MURPHY. But who is it that—who is the keeper of the definition that when you have a question——

Ms. HAMBURG. But our—our——

Mr. MURPHY. Who?

Ms. HAMBURG. Our chief counsel's office is——

Mr. MURPHY. Chief counsel. Have you reviewed with chief counsel the definition of "manufacturing" versus "compounding"?

Ms. HAMBURG. I think that everyone agrees that, at the present time——

Mr. MURPHY. I didn't ask you that.

Ms. HAMBURG [continuing]. That the law is not——

Mr. MURPHY. Please. Please, please, please.

Ms. HAMBURG [continuing]. Clear on this.

Mr. MURPHY. Please. I want to know, have you reviewed with someone—you said chief counsel—the definition of "compounding" versus "manufacturing"? Have you reviewed that with someone? When did that take place?

Ms. HAMBURG. You know, we have had many discussions on it, but the problem is——

Mr. MURPHY. So has someone reviewed with you a definition of "manufacturing" versus "compounding"?

Ms. HAMBURG. You know, I think that, really, you know, unfortunately, there is not a clear——

Mr. MURPHY. Yes, there is. Because in your authority—if you are telling us the crux of your testimony today is you don't have authority under manufacturing, you therefore must have met with someone who told you what the definition of "manufacturing" versus "compounding" is. I would like to know who that is. Or is it you?

Ms. HAMBURG. Well, you know, I really do think this is a broader issue. I know that you are frustrated by my answers, and I am sorry that I can't just give "yes" or "no," but this is a very complex issue. The courts of our country are split on these issues.

Mr. MURPHY. Ma'am, that is not complex. Complex is the life that the 32 victims' families have now. That is complex. What you have to do is easy, ma'am. Children growing up without parents, people without a spouse, living that lonely life, that, I submit to you, is complex.

Leadership is easy if you are willing to accept it. And you are not. Dr. Smith took leadership. She went in and cleaned house and identified problems.

What you are telling me is all this smoke and mirrors, that you don't have authority. Go look in the eyes of the victims, and try and comfort them with that. Ma'am, that doesn't work.

I am asking you a simple question, as everybody else has here. And you can't even tell us if you have talked to someone to come up with a definition of "manufacturing."

Ms. HAMBURG. No, I have told you we have been working very, very hard——

Mr. MURPHY. Tell us who——

Ms. HAMBURG [continuing]. To try to apply the authorities we have to an evolving industry and situations where we do not have the authorities we need. We don't even have registration of the compounding facilities to know who they all are. We cannot review the record. There are no Federal standards to which the compounding pharmacies are held. And the courts have not——

Mr. MURPHY. You should be able to provide us with a definition.

Ms. HAMBURG [continuing]. Been able to agree on what is the legal regulatory framework for examination of these problems and enforcement actions.

I care deeply about the patients and the families. The mission of the FDA is to promote and protect health. We are as frustrated as you are that we don't have the authorities and the resources——

Mr. MURPHY. Then just tell us the definition, ma'am. We will move from there.

I yield back. Thank you.

Mr. BURGESS [presiding]. The gentleman's time has expired.

The chair now recognizes the gentlelady from Florida, Ms. Castor, 5 minutes, for your questions, please.

Ms. CASTOR. Thank you very much.

And I appreciate all of us coming together to focus on what we can do to prevent tragedies like this from ever happening again.

Now, I do think it is clear that there is great ambiguity in the law. FDA—the law with regard to compounding pharmacies was last written in 1997; it is out of date. And from my colleague from Texas, there is ambiguity here, great ambiguity. And it has been made even more convoluted due to these court cases. And I wish we would bring this map up on the screen, as well, so folks watching outside this hearing room could see it.

See, in 1997 the Congress passed the FDA Modernization Act. That law contained a provision, section 503(a), which dictated the circumstances under which compounded drugs were new drugs and subject to FDA regulation. In that law, Congress explicitly exempted compounders from oversight and regulation as manufacturers. So I know that is what they are struggling with in trying to answer questions here.

Then the courts stepped in. And this is where I would like to follow up on Mr. Terry's question of you, Dr. Hamburg, about exactly which section of the act lacks clarity and his request that you direct him to it. We are talking here about the entirety of section 503(a), aren't we?

Ms. HAMBURG. Well, 503(a) applies in some areas of the country and not in other areas of the country, which is a very challenging situation——

Ms. CASTOR. Yes. Let's look at the map.

Ms. HAMBURG [continuing]. In terms of our ability to be as effective as possible.

Ms. CASTOR. Because in 2001, the ninth circuit, whose jurisdiction is the Western States, those red States, ruled that the advertising component of 503(a) was unconstitutional. And then they said that the rest of 503(a) is void because it is inextricably tied to the advertising component.

Then, a few years later, in 2008, the fifth circuit court, the blue States there to the south, whose jurisdiction includes Texas, Louisiana, and Mississippi, ruled that the unconstitutionality of the advertising restrictions did not affect the rest of 503(a). And, unfortunately, the United States Supreme Court did not speak to break the tie to provide clarity.

So, Commissioner Hamburg, what has been the impact on FDA in its regulation of compounded drugs as a result of these split court decisions?

Ms. HAMBURG. It has created a very challenging situation where we have, you know, contrasting legal regulatory frameworks for our actions. 503(a) applies in some places, and it does not—the other tool that we have is our compounding guidance that was written in 2002, but that doesn't have the force of law. It just lays out our best thinking about how to——

Ms. CASTOR. So then the States have primary responsibility over compounding——

Ms. HAMBURG. It is very clear that States have the day-to-day, routine responsibility for overseeing compounding facilities.

Ms. CASTOR. And then you have an industry that has evolved, that now some of the compounders, when you think of the pharmacy on the corner, where it is very important that a lot of our neighbors get their customized compounded drug, but some of them now are very sophisticated enterprises that are shipping all over the place, and they are not—they don't—they have outgrown the 1997 law.

So now we have to decide how we are going to update it to address the sophistication of compounders out there, and then go after these bad actors. Because I think the majority of these compounders are on the up and up, living up to high standards. But the compounding—this is the map from the compounding industry and association, and I am afraid that that has led to some of the bad actors being able to take advantage of this situation and the gaps in regulatory authority.

Is that a good summary? Is that an accurate summary?

Ms. HAMBURG. That is an excellent summary. And I appreciate your trying to help me explain this, because it is just an extraordinarily complex situation where, you know, the effort to——

Ms. CASTOR. Except I don't think that it is overly complex. I think there is a difference in outlook here on whether you have certain authority. And I think it is clear under the 1997 law and these court cases that compounders were exempted and are not manufacturers.

So we, the Congress, has the responsibility now to act and clarify it. And there has to be additional oversight of the States. If the States—if they are going to drop the ball and they are not—they are going—they are not going to provide proper oversight, then it is time for the Feds to step in and give FDA the tools it needs to prevent these tragedies from ever happening again.

Thank you. I yield back.

Ms. HAMBURG. I don't know if I am allowed to make a comment, but I think, you know, that speaking to the complexity of the issue and the changing, evolving industry overlaid on top of a fragmented and ambiguous legal framework, it is important to understand that this notion of sort of black and white, compounder or manufacturer, you know, it just is trying to fit a square peg into a round hole.

And, in fact, you know, if the law is examined, it isn't really adequately defined, but there is this area of outsourcing pharmacies that is increasingly important in medical practice. And if we were to define all of those pharmacies that hospitals now use—they used to make—Dr. Burgess, you would appreciate this. You know, it used to be that a hospital would add the potassium chloride to the

IV bag in their local—in their basement pharmacy or on the floor and give it to the patient. Now, both because of volume and, you know, concerns about making sure it is made under the best possible practices, that is outsourced to a pharmacy. They are making a product in larger volume and often not making it with a patient prescription in hand, yet it is, you know, clearly serving an important medical need.

And if we were to treat them as drug manufacturers, that would be simply impossible. They would have to submit an application, a formal application, to FDA for review and action. They would have to pay fees associated with that, as well. They would have to be subject to good manufacturing practice.

And so I think we want to work together to make sure that we have a law that clearly defines critical issues and authorities, that enables important patient needs to be addressed, but clarifies the different roles and responsibilities, and puts in place some critical authorities that are currently missing.

Mr. BURGESS. I am going to interrupt you there in the interest of time. Dr. Gingrey has been waiting patiently.

And, Dr. Gingrey, you are recognized, 5 minutes for questions, sir.

Mr. GINGREY. Mr. Chairman, thank you very much.

And, of course, an extremely interesting and important hearing. Tragic in so many ways, of the lives lost and the number of cases of meningitis as a result of this bad actor.

Dr. Hamburg, Dr. Smith, pediatricians both, we appreciate your being here.

And some of the questioning, the line of questioning from both sides of the dais, both Republicans and Democrats, have being pretty tough, but they have to be. Because if we are going to change the law, if we are going to rewrite the Federal Food, Drug, and Cosmetic Act, particularly in regard to section 503(a) and the vagueness of that section and the conflicting court decisions, then we have to get this right. And I have some great concerns that we might not get it right, in regard to overreacting in regulating compounding pharmacies.

Every Member of the House of Representatives have drugstores. And they are not chain drugstores; a lot of them are just corner druggists that do compounding, where a certain product is needed by a patient, but maybe the manufactured product, it is in a base or something that they are allergic to, so therefore the local pharmacist has to reconstitute that drug—not manufacture a drug; the drug is manufactured—and just put it in a different way of giving it to the patient. It might even be in a pellet form. Think hormone replacement therapy, in some cases, or a cream or a vanishing cream or something that the patient is not allergic to.

So if we get to the point in the line of questioning that Dr. Hamburg received from our longstanding member emeritus, Mr. Dingell, about compounding pharmacies, that worries me a little bit, that we might overreact and get to the point that we are not getting at the problem.

It seems to me that this particular company, this New England Compounding Company, was an unusually bad actor, unusually egregious. And I would be very surprised if there are not multiple

lawsuits and, in the final analysis, some folks serving some jail time.

And, you know, again, I can't understand why—Dr. Smith, I will direct this to you. I realize you have only been in this position for a few months. And by all appearances and from what I read, you are doing a commendable job. But, gosh, this company is going back to 1998, and a bright light has been shining on it at least since 2002. And there has to be some connection between members of this Massachusetts Pharmacy Board, I guess appointed by the Governor, I don't know for what period of time. And I think we have some evidence that there was some cross-pollination, where maybe even one of these individuals served on the board of the New England Compounding Center or one of these sister companies. And, you know, it is just unbelievable.

The general public is so disgusted with Washington. I mean, you look, we are reading about what is going on now at the highest level of our military. And this situation where, in the 21st century, we have a Food and Drug Administration and we have State pharmacy boards, that something like this could happen. It is, like—it is almost beyond belief.

But it makes me think back to what President Reagan said in reference to the Russians and their nuclear stockpile: "Trust, but verify." And that is the responsibility of this committee, this Oversight and Investigations Subcommittee of Energy and Commerce. Trust, but verify. And we are not very trusting today, as you can tell from our line of questioning. And we shouldn't be.

That judge, his widow in the previous panel talked about his contribution to society in the great State of Tennessee. And his life was lost, but he was just one of how many? Well, we are talking about far too many people.

So I would just in my last second ask you, Dr. Hamburg—and maybe Dr. Smith could comment, as well—do you think that the FDA needs, because of this, to all of a sudden have us change the law so that you and the FDA, or whoever succeeds you, has this broad authority over these little compounding pharmacies all across the country who are doing the right thing? They are not manufacturing drugs; they are just trying to provide a service, indeed, based on a prescription that has to be written.

This company was an absolute crooked operation, and they killed people. But I don't think anybody here should get confused between them and the typical compounding pharmacist at our corner drugstores all across our districts.

Ms. HAMBURG. Yes. Well, I think we need a tiered approach, and that is what we are proposing in terms of the need for new legislation. I think that, clearly, the traditional compounder working locally is most appropriately overseen by the State. But this isn't, sadly, an isolated incident. This is the worst and most tragic, and it should be the last wake-up call to us. But over a period now of, you know, almost two decades, there have been problems with compounding facilities, compounding pharmacies.

And I think it reflects this gap in regulatory oversight and the fact that we really need a strong, clear, and appropriate legislation. We cannot have a crazy quilt where different parts of the country are subject to different legal frameworks for oversight. We need a

tiered system that recognizes the role of traditional compounding and the role of the States; nontraditional compounding, which represents higher risks, and there should be Federal standards.

And we need to look at a set of statutorily based criteria, factors that in some combination would put people into this category: the type of product or activity, whether it is sterile processing, for example, the amount of product being made, whether it is in interstate commerce, whether it is going directly to the end-user or through a third party, and the nature of the anticipatory compounding.

And then there are some things that just simply shouldn't be compounded, that should be manufactured by drug manufacturers subject to the full force of FDA authorities. And that would include, you know, certain things that you are well familiar with: extended release, transdermal, biologics, and other kinds of products that, because of the nature of the manufacturing, they really should be made in accordance with good manufacturing practice. They should be subject to the FDA preapproval review for safety, efficacy, and quality manufacturing——

Mr. GINGREY. Dr. Hamburg, thank you. I have gone way beyond my time, and I really appreciate the chairman's indulgence. And I yield back.

Mr. STEARNS [presiding]. Sure.

The gentleman from Texas, Mr. Green, is recognized.

Mr. GREEN. Thank you, Mr. Chairman.

I think the questions and the testimony here today showed from all three panels the problem we have. The NECC tragedy laid bare a regulatory gap that we have between the practice of traditional pharmacy compounding and full-scale drug manufacturing.

There is no debate that we want the Federal Government to license individual pharmacists. That is a State responsibility. Nor is there a debate about whether FDA should oversee large-scale manufacturing of drugs, which is I think on a bipartisan basis what we have heard.

There have been overwhelming numbers of signals, though, about NECC, which is not your average neighborhood pharmacy.

Commissioner Smith, how many different States did NECC sell their products to?

Ms. SMITH. I am not sure about all of their products, but in terms of——

Mr. GREEN. But they did sell it into a lot of States. Did they did sell it into Massachusetts?

Ms. SMITH. Yes, they did. Twenty-three, I believe, is where they——

Mr. GREEN. Twenty-three States? But did they sell their products in the Massachusetts market?

Ms. SMITH. Yes.

Mr. GREEN. OK. How many States did it send the contaminated injections that led to the outbreak?

Ms. SMITH. That was the 23.

Mr. GREEN. OK.

Ms. SMITH. They may sell into more, but that was the 23.

Mr. GREEN. NECC was not new to this nationwide shipping. Hadn't they been operating throughout the company—the country for about a decade?

Ms. SMITH. That is correct.

Mr. GREEN. The Massachusetts Board of Pharmacy had been getting complaints and troubling sings from States around the country for that whole period of time. The board received complaints from Idaho and New York that NECC was inappropriately soliciting business. The board received a report from South Dakota pharmacists that NECC was sending blank forms for dosage size that you never use on one person. The board received adverse event reports from NECC products from Florida and New York. And the board received complaints from pharmacists in Texas and Iowa on how NECC was soliciting and filling prescriptions. The board also received reports of cease-and-desist orders for NECC for in Colorado.

Dr. Smith, red flags came from across the country, and I can go over that list of States again. Wasn't it obvious that NECC was operating on such a large scale that it presented a nationwide problem of a sort that warranted greater involvement by the Federal Government?

Ms. SMITH. Yes.

Mr. GREEN. Did the board in Massachusetts request any assistance from the FDA?

Ms. SMITH. I am not aware of any specific requests. However, there were—certainly, during this most recent outbreak, we have worked together, and——

Mr. GREEN. OK. But they have been doing this for 10 years. And you all have records of it. Did you share those records with the FDA, those complaints?

Ms. SMITH. I am not aware—I do not recall. I would have to look back to check, so I don't know the——

Mr. GREEN. Well, and I think that is our problem. And I have been on the committee since '97. We never included Federal regulation or compounding pharmacists because, frankly, I don't—that is licensing, and that is the State. But when they are in the manufacturing situation, which they are, then that means they should have been covered by Federal law.

And I know it is complicated and it is hard for a doctor to explain legal; it is hard for lawyers to explain some of the legal theories that the courts do. But that is the decision I think Congress needs to make. And I think we have a bipartisan agreement, this subcommittee doesn't do legislation. But, believe me, the Health Subcommittee can.

And I don't know if we can do it by the end of the term. And I know our chairman is not here, and even our ranking member. But I would hope that we could look at a very quick piece of legislation that we could have a hearing on and to correct this problem.

Because if you are a compounding manufacturer in Texas and selling in interstate commerce, it ought to be Federal law covering it. I don't expect our local pharmacy board in Texas—they go around and inspect my pharmacists, whether they be in the large pharmacies like Walgreens, in our case, or CVS, I know a Rite Aid here, or our neighborhood pharmacists. But they don't inspect, nec-

essarily, the compounding manufacturers. And that is where Federal law needs to come.

And I will be glad to yield to my colleague, and I would hope that we would see movement on the bill on a bipartisan basis. Thank you.

Mr. MARKEY. Thank you.

Let me ask you this, Dr. Hamburg, when you try to inspect compounded drugs, do you get sued by the compounding industry?

Ms. HAMBURG. We have been sued on numerous occasions, and we have been challenged in terms of our authority.

Mr. MARKEY. When you try to regulate compounded drugs as new drugs, do you get sued by the compounding industry?

Ms. HAMBURG. We do not. The authority there is very clear, the expectations on drug manufacturers in terms of what they need to do to comply with FDA law.

Mr. MARKEY. When you request documents from compounding firms, do they sue to block you from getting——

Ms. HAMBURG. You know, we often have to go to the courts and get warrants in order to get the materials that we need. We do not have the full authority that we need to review documents.

Mr. MARKEY. When you are asking a drug company, Merck, when you request documents from them, do they go to court?

Ms. HAMBURG. No, we have much clearer authority over drug manufacturers.

Mr. MARKEY. When you are inspecting Merck, do they question your authority to inspect?

Ms. HAMBURG. No, they do not.

Mr. MARKEY. And that is why she needs authority. That is why the FDA needs authority. Because it is clear that the drug companies accept the law and the FDA's authority.

Mr. GREEN. As much as I agree with my colleague from Massachusetts, I yield back my time, but I would hope our committee hearing has done what we need to do and can encourage——

Mr. STEARNS. Will the gentleman—I think his comments were very appropriate and bipartisan, and I appreciate that.

Do you think in your heart of hearts that the Energy and Commerce Health Subcommittee should provide more regulation and authority to the FDA before the end of the year?

Mr. GREEN. I think we ought to respond to the tragedy that happened, and I think we owe it to the families, but also to probably thousands of people who may not have been subject to a death in their family but an illness because of the practices of this particular compounding company. It happens to be in Massachusetts, but it could have been in any other State. But Massachusetts did have warning. There were complaints for 10 years about it.

And I would hope that we would have better interstate sharing between the States and the Federal regulatory agencies, even though they may not have had the authority, but somehow, in 10 years, they could have come to us and maybe we could have given it earlier.

Mr. STEARNS. I thank the gentleman.

The gentleman from Virginia, Mr. Griffith, is recognized for 5 minutes.

Mr. GRIFFITH. Thank you, Mr. Chairman, I appreciate it, and obviously, this is very frustrating. You know, I would like to know what kind of due diligence the FDA has the authority to do? Do you send out letters to doctors saying, where are you getting your compound medicines from, or where are you getting your supplies from? And the reason I ask that, and the same thing for hospitals, or clinics, or other medical providers, because this was not what we think of as compounding. This was manufacturing. In my small area, which is, you know, it overlaps the Roanoke Valley, the New River Valley, we have compiled a list of approximately 1,415 patients who were advised based on press reports, they were notified they could have been exposed to fungal meningitis through the tainted steroid injections and other products made by the New England Compounding Center, and we have, you know, a hospital that didn't, fortunately, use it, but had it sitting on the shelf. We had—that was at the Carilion Giles Community Hospital. We had the Insight Imagining in Roanoke and the New River Valley. We had other clinics, including Vista Eye Center, LewisGale Medical Center in Salem, and Carilion Roanoke Memorial, all of which had these products.

And when you have that many, you know, I don't represent New York City. This is a fairly, compared to other parts of the country, a fairly small area, and we have got 1,415 people who have to worry about whether or not they are going to get the disease. We have more than that who have already contracted it, roughly 50 confirmed cases in the area. Three of those, so that I am being fair, were across the line in West Virginia, but not that far from our medical centers. And when you have got that many folks affected, we are not dealing with a compounder, which is why it has been frustrating all day, I think, for members of this committee, when you keep going, our jurisdiction is not clear. Your jurisdiction was clear; these folks were manufacturing.

Now what due diligence did you take to find this out? Because these are all pretty big operations, and if you just sent them a letter saying, hey, who is providing you with various products? You know, I think they would have complied, and you would have had then the, you know, you didn't—FDA, not you—but did some work back under the Bush administration, but then it appears that the ball was dropped and that there was no—it appears there was no due diligence going on that you all weren't saying, hey, who is providing you with this stuff? Because you know what, we have got Colorado involved; we have not Tennessee involved, who made complaints in advance. And we have got 1,415 people who either live in my district, or Bob Goodlatte's predominantly, and you know, somebody wasn't paying attention.

These were not our compounding. This was not your small compounding pharmacy. These were, in fact, manufacturers. And I recognize they were violating the laws, but it is very frustrating when you come in here and say, our authority wasn't clear. These folks were manufacturing. And what are you doing now to find out if there is somebody else out there who is manufacturing under the claim that they are not, I mean, you know, spending——

Ms. HAMBURG. Well, I think your question speaks directly to why we do need legislation and new authorities. Compounding pharmacies are not required——

Mr. GRIFFITH. All right, hang on, I am not worried about compounding. I am telling you that from the evidence I have heard today, it appears that these were manufacturers. So what do you all do to find out if somebody is manufacturing illegally, because that is what I think we have here? And you keep going back to compounding, and that is why everybody is getting frustrated with you; 1,415 cases, you know, a number of States away is not a compounder. That is a manufacturer.

Ms. HAMBURG. Well, I think we really do need to clarify that in legislation in terms of——

Mr. GRIFFITH. All right. I already heard that. Let me go on to another question because I have limited time like everybody else does.

There was marketing going on, and I am going to switch to you, Dr. Smith. There was marketing going on. They apparently were aggressively marketing bulk pricing, discounts to the clinics. You are aware of that at this point?

Ms. SMITH. Well, yes, those were some of the claims, or the issues that had come up before.

Mr. GRIFFITH. OK, and I guess if they are aggressively marketing to multiple States, did it—are there any memos, I know you weren't there, and I appreciate you coming forward and saying, look, mistakes were made. Did anybody think, hey, wait a minute, this is not traditional compounding, this is a manufacturer, we need to turn this over to the FDA and let them deal with them as manufacturers? Because that is what the evidence—notwithstanding the FDA not wanting to accept some responsibility today at all, that appears to be what happened here, is that somebody was violating the law, and pulling a fraud and claiming they were compounders when they were in fact manufacturers. Did that ever come up in any of the notes or the memos that you have seen thus far?

Ms. SMITH. It hasn't come up, or we haven't found that level of conversation. What has been clear and remains clear, is that Massachusetts law requires one prescription per patient. And so the issue that has come up as you describe it, is that clearly you can't do that and still do one prescription per patient.

Mr. GRIFFITH. Right.

Ms. SMITH. One of the things we have done since this all has come to light is to, A, remind all pharmacies in Massachusetts of that; remind hospitals that if you are getting product, that it needs to be one prescription per patient, for exactly the reasons that we have been discussing.

Mr. GRIFFITH. Well, I appreciate that.

And Mr. Chairman I know my time is up, and I appreciate this hearing being held. Earlier today you said, or somebody said there would be more hearings. I certainly hope there are, and I hope that we can get some answers on why and what we need to do, not on the compounding side but to make sure the FDA has authority, because apparently, they don't, to just check and see if we have peo-

ple out there who are committing fraud on the public by claiming to be a compounder when they are in fact manufacturers.

Mr. STEARNS. I thank the gentleman.

And I say to all the members we are going to go for a second round. I talked to the ranking member, she has agreed. It is not necessarily going to be the full 5 minutes, but if you—if the panel will be patient with us, there are no votes today, so we do have this unique opportunity to have a second round.

I want to continue with a little bit what Mr. Griffith indicated. He sort of indicated going forward today, have you come up with procedures and interpretations so that the manufacturers out there that are doing the same thing as NECC, that you can stop them? And I didn't—you didn't seem to give a clear answer. So what assurance do we have in the public mind and legislators that the FDA is going to prevent this from happening today because we might not get legislation? This is a lame duck session, but the Republicans control the House; the Democrats the Senate. I mean, it is going to be very difficult to get legislation through normally, even though this is a very serious problem, and I think we are all bipartisan on this. Sometimes between the cup and the lip, it takes a while. So I think what Mr. Griffith was touching on is, what assurance can you give the public that the other NECCs that are out there, that you are going to stop them?

Ms. HAMBURG. Well, I do want to underscore that I believe that we need legislation——

Mr. STEARNS. So you cannot stop them unless you have more legislation?

Ms. HAMBURG [continuing]. To sanction and clarify authority. In the interim, we are working very hard, working with our colleagues at the State. I mentioned that we are actively engaging with the States in order to both provide our best possible information about best practices, et cetera.

Mr. STEARNS. Do you feel confident you could stop another NECC; with the jurisdiction and the understanding you have now, could you stop another NECC who is manufacturing drugs? Could you stop them today?

Ms. HAMBURG. NECC was not the first, and it will not be the last——

Mr. STEARNS. OK. All right.

Ms. HAMBURG [continuing]. Until we work together to clarify and strengthen the laws that surround——

Mr. STEARNS. Dr. Smith, you indicated in your opening statement that because of what happened, people have been fired and suspended. Is that true?

Ms. SMITH. Correct.

Mr. STEARNS. And you have also implemented new regulations and new oversight interpretation so that you can prevent this from happening again, is that correct?

Ms. SMITH. Yes.

Mr. STEARNS. OK. Dr. Hamburg, have you fired or suspended anybody at the FDA because of this tragedy? Yes or no?

Ms. HAMBURG. No.

Mr. STEARNS. OK, have you gone through, introspectively, looked at the agency and said, these are the regulations, these are the

things we need to do to prevent another NECC? Have you done that?

Ms. HAMBURG. We have done that. We have been working very hard to identify what are the authorities that we need to be able to protect the American people and to help to ensure that they get the quality drugs that they deserve.

Mr. STEARNS. With the NECC incident, is it your position today that this could have been prevented by the Massachusetts Department of Public Health? Yes or no?

Ms. HAMBURG. I believe that we need a stronger regulation framework——

Mr. STEARNS. No, could they have, in your opinion——

Ms. HAMBURG [continuing]. But I believe that different actions might have been taken with NECC that could have——

Mr. STEARNS. See, the problem is that you are saying——

Ms. HAMBURG [continuing]. Prevented it, and I wish that that were so, but I think we just have to look at the record, that there has been——

Mr. STEARNS. Did somebody tell you to filibuster us? Is that why you are handling the questions——

Ms. HAMBURG. I apologize but, you know——

Mr. STEARNS. No, the question is——

Ms. HAMBURG [continuing]. This is an important issue, and I care about it.

Mr. STEARNS. You are saying you did not have the authority to stop this, is what you keep saying today; you don't have the authority to do it. Do you think that Dr. Smith's agency should have stopped it? Just yes or no. If you don't know, just say you don't know.

Ms. HAMBURG. Well, I think that clearly, Massachusetts was working very hard.

Mr. STEARNS. So you think they could have stopped it, and you didn't have to stop it.

Ms. HAMBURG. They were unsuccessful, and it is, you know, was tragic. We worked hard with them to limit the——

Mr. STEARNS. OK. OK. I understand.

Ms. HAMBURG [continuing]. Outbreak, and we want to work with you.

Mr. STEARNS. I have two more questions for you here. Is it your position today that the NECC was not a manufacturing pharmacy and that you had no jurisdiction over its business activities? Is that your position today?

Ms. HAMBURG. NECC is——

Mr. STEARNS. Yes or no.

Ms. HAMBURG [continuing]. Registered as a compounding pharmacy.

Mr. STEARNS. No, I am talking about NECC. Did they, in your opinion, in your opinion, this is the crux of the hearing now, it is your position today that the NECC was not a manufacturing pharmacy, and you had no jurisdiction over its business activity? Is that your position today? Yes or no?

Ms. HAMBURG. No, that is a subject of an ongoing investigation.

Mr. STEARNS. No, but you have been telling us all day today——

Ms. HAMBURG. I cannot characterize.

Mr. STEARNS [continuing]. That you had no jurisdiction, it is murky?

Ms. HAMBURG. I cannot characterize that while there is a criminal investigation that is underway.

Mr. STEARNS. Let me get more pointed. Is it your position today that the FDA could not have prevented this tragedy because you did not have jurisdiction, is that what you are telling me today?

Ms. HAMBURG. I, you know——

Mr. STEARNS. Yes or no?

Ms. HAMBURG. I am sorry, we can speculate——

Mr. STEARNS. You are in charge of the FDA. You are the chief honcho. You are the great poobah of the FDA, and I am asking you, basically, could you have prevented this tragedy, and you are saying you can't because you didn't have jurisdiction.

Ms. HAMBURG. It is very hard to know if any one action that we might have taken could have stopped this terrible tragedy. I wish that I could identify what that would be. What I can't——

Mr. STEARNS. FDA did nothing wrong, in your opinion?

Ms. HAMBURG. No, what I am—I am not saying that.

Mr. STEARNS. In 2002, when they inspected and found all of the problems, and 2006, when they wrote the letter and said, we are going to shut you down; I mean, all of that is just too murky for you, and you don't think the FDA has any responsibility?

Ms. HAMBURG. No, this is—this is not a forum, unfortunately, that enables us to speak to the——

Mr. STEARNS. Well, you can speak it pretty well. We have given you lots of time.

Ms. HAMBURG. I think that, you know, what we really want to do together is make sure that this kind of event——

Mr. STEARNS. Oh, that is axiomatic. We all understand that, but the question is, we are trying to say that—we are trying to understand how this could be prevented, and you are saying you don't know how it could have been prevented by the FDA.

Ms. HAMBURG. I think that——

Mr. STEARNS. You are not even—you haven't fired anybody. You haven't suspended anybody. It is not even clear that you have actually initiated anything, so I think we are leaving with the impression that thank goodness that Dr. Smith stepped up to the plate and did something, and we are just a little unsure what you are going to do. In fact, according to the staff, we are waiting, as Mr. Dingell said, we are waiting for all of this information from your agency, and we didn't even get assurance when you were asked by the chairman and by Mr. Dingell that we are going to get all this information. I am telling you, there is so much out there that your agency has not given us, in all deference to you, Madam. I mean, you have only been there a short time, I appreciate that. We need your assurance that you will provide it.

Ms. HAMBURG. We will provide the information that you have requested.

Mr. STEARNS. OK, my time is expired.

Mr. STEARNS. Go ahead, Ms. DeGette.

Ms. DEGETTE. I am pulling myself together. I am going to ask some questions.

Dr. Hamburg, I think you can agree with me that, between 2002 and 2006, the FDA made some attempts to investigate this, and they were pretty inconclusive, correct, yes or no? Yes or no?

Ms. HAMBURG. I apologize——

Ms. DEGETTE. OK, you are not going to answer that. Let's just keep going on. OK, now, in April of 2002, the FDA began an inspection of the New England Compounding Center, correct? Yes or no?

Ms. HAMBURG. Yes.

Ms. DEGETTE. And that inspection continued throughout the fall and winter of 2002 and 2003, correct?

Ms. HAMBURG. Correct.

Ms. DEGETTE. Now, eventually, now, you weren't there. This was not your—it was not your job to defend what they did. But in 2002, the FDA investigators concluded, after a lot of investigation, that they—that there were jurisdictional issues, is that correct, yes or no?

Ms. HAMBURG. That is correct.

Ms. DEGETTE. They then turned this investigation—there still was some FDA involvement, but for the most part, they turned this investigation over to Massachusetts, yes or no?

Ms. HAMBURG. Yes.

Ms. DEGETTE. And so what happened at that point was then the FDA did have some involvement, but it was primarily Massachusetts, is that right? Yes or no?

Ms. HAMBURG. That is correct.

Ms. DEGETTE. Now, in the meantime, you know, I will say we are just trying to get answers here because we do need to figure out how to prevent this. And if we can't prevent this kind of a thing, then shame on us, because this is a company that had black specks floating in the vials. It had cleanliness that wouldn't even be accepted anywhere in the world. And we are all sitting here wringing our hands. So we have to figure out how to give you the jurisdiction to do what you need to do, and we have to figure out how to give Dr. Smith and all of the other State regulators, like Colorado, the ability to work with you to do that. OK?

Ms. HAMBURG. Agreed.

Ms. DEGETTE. And these inconclusive answers are not helping us. Now, the act, Section 503 of the act has all of these requirements regarding the compounders, correct?

Ms. HAMBURG. Correct.

Ms. DEGETTE. And what it says is, a compounded drug is exempt from a variety of requirements of the Federal Food, Drug and Cosmetic Act relating to drugs to get FDA pre-approval if the drug is compounded for an individual patient based on the unsolicited receipt of a valid prescription, correct?

Ms. HAMBURG. Correct.

Ms. DEGETTE. And it says, the drug is compounded by a licensed compounding pharmacy, correct?

Ms. HAMBURG. Correct.

Ms. DEGETTE. So what has happened over all of these years is these drug compounders have started these great big manufacturing facilities, and then they have the illusion that they are keep-

ing these scripts for the individual patients, but they are really not doing that. Is that correct?

Ms. HAMBURG. That is correct.

Ms. DEGETTE. And that is part of the problem, right?

Ms. HAMBURG. That is.

Ms. DEGETTE. OK, now, just hold off. So the other thing that has happened then, Section 503(a) says, and this goes to what Mr. Griffith was saying, is Section 503(a) says that the FDA can take jurisdiction if these compounding pharmacies are exporting more than 5 percent of their drugs to other States, correct? It says that, right?

Ms. HAMBURG. 503(a), yes.

Ms. DEGETTE. So what Mr. Griffith is saying then, is why doesn't the FDA just enforce that? But here is the problem, Mr. Griffith, and this is what Commissioner Hamburg is trying to say. Is the Ninth Circuit has thrown out all of Section 503, and it says, it doesn't even apply. And the Fifth Circuit has said Section 503(a) only applies to advertising, and that is what that map is about.

And so what Dr. Hamburg is trying to say is, you know, we can point fingers and we can be upset, and everything, and we should be, about what happened 10 years ago, and why this operation wasn't shut down, but what we really need to think about is what are we going to do going forward to make sure that the jurisdiction is clarified?

And I would bet you if we could all sit down and talk about it, we could agree on the same principles. We don't want the FDA having jurisdiction over the doctor and the little mom-and-pop pharmacy who is trying to make the ointment for the kid. But if it really is a big manufacturing operation, even though it is a compounding pharmacy, we need to, if the law isn't clarified now, if there is litigation, if there is a separation of court decisions in the cases, we need to fix that. And that is our job as Congress.

So I guess I would say, Dr. Hamburg, you know, I understand what you are saying, but within the—within the purview of the law as it is written now, the FDA needs to do everything it can to make sure it prevents this kind of activity. And furthermore, we have a job, we have a job to all of these victims as Congress to not try to move the lounge chairs around on the Titanic.

We have a job to clarify the law if there is not clarity in the law, and we can easily do it. So thank you, Mr. Chairman, and I yield back.

Mr. STEARNS. I think we have a little time here. We could—you and I could have a colloquy here, and Mr. Griffith, you can participate in this colloquy. You are an attorney, Ms. DeGette, and I appreciate what you are saying, but I think the interpretation of what you did on the Supreme Court is not wholly explained, as you said. I am asking staff, did the Supreme Court throw out the entire was it 503(a). I don't think they threw it out. They threw out only that portion that dealt with marketing. And so for you to say they threw out the whole thing so that the commissioner and the FDA had no interpretation——

Ms. DEGETTE. No, no that is not what I said, Mr. Chairman.

Mr. STEARNS. Well, that is what you sort of implied, and the legal problem is that the Supreme Court only did a very small portion of that and left intact the idea that the company that is manu-

facturing still can be determined if they are a small pharmaceutical or they are a manufacturer, so I would submit——

Ms. DEGETTE. Mr. Chairman, if you would like to have a colloquy, I will tell you what I said.

Mr. STEARNS. I think you appreciate what I said.

Ms. DEGETTE. What I said was that the Fifth Circuit threw out the 503(a) provision only on advertising, and left the rest of it intact.

Mr. STEARNS. Right.

Ms. DEGETTE. The Ninth Circuit threw out all of 503, and then the Supreme Court took cert on the Fifth Circuit—Ninth Circuit case, but they only talked about the advertising. So now it is really a big mess.

Mr. STEARNS. And I agree, because of the Fifth, and Ninth Circuit, and the Supreme Court. But I don't think, and this is what you are implying, that it creates such a position that the FDA had their hands tied, and they couldn't determine what is a manufacturing and what is a small pharmaceutical. I think you still have——

Ms. DEGETTE. Again, you are misinterpreting what I said.

Mr. STEARNS. OK.

Ms. DEGETTE. What I said is that there is a lack of clarity in the law and what that means is that evil-doers like this compounding pharmacy, don't feel like they have to listen to the FDA. They don't feel like they have to produce the documents when they are requested, and they sue whenever there is anything that happens. And that is the problem, is it ties the FDA's hands when they are trying to take enforcement actions against these folks even if they want to.

Mr. STEARNS. OK, you are welcome to step in here, but I think I would——

Mr. WAXMAN. Point of order, Mr. Chairman. Whose time is it now?

Mr. STEARNS. Right now, it is hers. I gave her the time, and she yielded back, and I asked her if I could have a colloquy with her, which she agreed to, and you are welcome to join in. I think this is a legal interpretation, which I think you are welcome to join in.

Mr. WAXMAN. Mr. Chairman, I wouldn't want to interrupt your discussion, but we do have members on both sides of the aisle waiting for their opportunity to get to the round of questions.

Mr. STEARNS. Oh, sure, well, you weren't here at the time, and I would be glad to recognize you.

Mr. WAXMAN. It goes to your side next.

Mr. STEARNS. Oh, that is right. You are right. I am going to take 15 seconds and just say the purview of the chairman is I think what Ms. DeGette is talking about between the Fifth and the Ninth Circuit Court, and the Supreme Court——

Ms. DEGETTE. Don't interpret what I am saying.

Mr. STEARNS. I know, but I am the chairman, and what I think is that there was still left the integrity of the law so that the FDA could determine who is manufacturing and who they have jurisdiction over.

Mr. WAXMAN. Regular order, Mr. Chairman.

Mr. STEARNS. With that, I will recognize the gentlelady from Tennessee.

Mrs. BLACKBURN. Thank you, Mr. Chairman, and I have just a couple of questions.

You all have stayed with us, and I do appreciate this.

A point of clarification, Dr. Hamburg. You mentioned earlier there are 7,500 advanced compounding pharmacists and 3,000 sterile.

Ms. HAMBURG. That is information that was given to us by the International Association of Compounding Pharmacies.

Mrs. BLACKBURN. OK, well, that is what I want to know if that was——

Ms. HAMBURG. We don't know the numbers because they are not required to actually report to us, so we don't know numbers from our own assessments.

Mrs. BLACKBURN. OK, but you can source that for us? Would you provide that sourcing so that we have that?

Ms. HAMBURG. OK, certainly.

Mrs. BLACKBURN. OK, thank you, I appreciate that. Let me, I want to go back to this issue that you all had because you had the Colorado complaint against NECC in May of 2011, is that correct?

Ms. HAMBURG. That is correct.

Mrs. BLACKBURN. OK. And that complaint came into you well in advance to any of these contaminated lots being shipped, is that also correct?

Ms. HAMBURG. Well, as I understand it, it was a request for information from us about whether they were registered as a manufacturer, a drug manufacturer, and they—NECC is listed as a compounder.

Mrs. BLACKBURN. Well, I think Colorado notified the same FDA compliance officers who had inspected NECC in the past, is that correct?

Ms. HAMBURG. I believe.

Mrs. BLACKBURN. And that these inspectors were aware of NECC's past violations, isn't that correct?

Ms. HAMBURG. I believe that the email from Colorado was shared within the FDA because of the history with NECC.

Mrs. BLACKBURN. OK, and then, in that email, did they not say that NECC was again shipping volumes of drugs without a prescription?

Ms. HAMBURG. What they indicated to us was that they were concerned that NECC was operating in violation of Colorado State Board of Pharmacy licensure and registration laws, and they included attachments——

Mrs. BLACKBURN. OK. Doctor.

Ms. HAMBURG [continuing]. About the volume of product that was being shipped.

Mrs. BLACKBURN. But it was clear that it was a repeat violation, isn't that correct?

Ms. HAMBURG. What was clear was there were not specific safety and quality concerns, but they were noting that there were not valid prescriptions for the materials that were being sent to Colorado.

Mrs. BLACKBURN. OK, let me ask you this. Did the FDA do anything at all with that complaint?

Ms. HAMBURG. Well, we suggested that they follow up with the Massachusetts Board of Pharmacy because——

Mrs. BLACKBURN. You suggested? You suggested; you didn't require. Did you even pick up the telephone and call the Massachusetts Board of Pharmacy and say, "We think we have a repeat offender"?

Ms. HAMBURG. I understand, you know, what you are getting at there, but it——

Mrs. BLACKBURN. Yes or no. Did you pick up the phone and call? Did anybody pick up the phone and call?

Ms. HAMBURG. Email was being used, but it was communicated through the Colorado Board of Pharmacy.

Mrs. BLACKBURN. Would you like to supply all of those emails to us for the record?

Ms. HAMBURG. I believe you have them.

Mrs. BLACKBURN. OK, we have got all of those in total. When did you personally become aware of the situation? I mean, at what point in the process did you individually, not your staff, but you? When did you hear of it.

Ms. HAMBURG. When the first cluster of meningitis cases and the possible link to NECC was identified. It was in late September.

Mrs. BLACKBURN. OK, Dr. Smith, let me come to you with my last minute. Did the FDA ever contact you?

Ms. SMITH. Are you—just so I can understand, do you mean in the past or around this current outbreak?

Mrs. BLACKBURN. No, let's go back to the Colorado complaint. Did they ever contact you? Did you ever—did you ever get a phone call or an email from anybody that said, we think we have a repeat offender out here?

Ms. SMITH. Well, I can't speak to the phone calls, but review of the emails does not suggest that we got any information then.

Mrs. BLACKBURN. So they knew they had a repeat offender, but they did not call you.

With the boards of pharmacy, like with Colorado, back to you, is there any direct contact there? You know, so many of our State boards, who do a great job of regulating areas, contact and work with other State boards who have like supervision in their States.

Ms. SMITH. Well, we did receive information from Colorado about the action, but it wasn't until July of 2012, and we weren't, or I wasn't aware of that until we discovered that in the process of producing the documents for this committee.

Mrs. BLACKBURN. OK, and let me ask you this: Personnel actions in response to this, the NECC, have you taken any actions there?

Ms. SMITH. Yes, the executive director at the time has been let go from the department, and the board counsel has been put on administrative leave as was the division director for that area.

Mrs. BLACKBURN. And are you reviewing your processes and best practices?

Ms. SMITH. Regarding personnel actions?

Mrs. BLACKBURN. Yes.

Ms. SMITH. Yes, as we reviewed the information, again, that we presented for this committee, we have identified lapses in judgment, which have resulted in these personnel actions.

Mrs. BLACKBURN. Thank you. I yield back.

Mr. STEARNS. The gentleman from California, Mr. Waxman, is recognized for 5 minutes.

Mr. WAXMAN. Thank you, Mr. Chairman.

I find this hearing amazing.

Mr. STEARNS. Amazing.

Mr. WAXMAN. Because what we need to do is to work together to solve a problem and make sure it will never happen again. Instead what I hear from my Republican colleagues is they want to prosecute the director of the Food and Drug Administration. Did she know this? What action did she take?

It sounds like Massachusetts has a lot to be apologetic about. Isn't that a fair statement, Dr. Smith.

Ms. SMITH. Yes, you are right.

Mr. WAXMAN. And the question is, did FDA fail to do things they should have done? Well, it sounds like you could have done more. The FDA as an institution could have done more. The first time they wrote a letter was in 2006, saying that this thing seemed to be—this company seemed to be out of control. And then they didn't do anything after that.

Now, I have a feeling, Dr. Hamburg, you are being picked on because you are part of the Obama administration, and Republicans have been picking on Obama for 4 years, and usually their mantra goes, job-destroying regulation, let industry police itself, we don't want government involvement.

Now, they are saying, we want more government involvement, and I think they are right. We want appropriate government involvement to stop these things from happening.

So you would think that our obligation would be to figure out, do you have the authority? I respect the chairman greatly, but I have never understood him to be a great legal scholar. It seems to me there is some ambiguity. If there is an ambiguity it is our job to clear it up. You think there is an ambiguity because the law that we drafted in 1997 said one thing and the court came in and said something else. You don't know whether you can act, whether you can't act. If we want to make sure you act in the future, other than just beat you up for not acting, we ought to make sure that you have all of the authority appropriate to act. The courts have thrown out part of that 1997 law. The courts are themselves divided on whether Section 503(a) continues to have any legal force. In the Western States, 503(a) is not effective; while in Texas, Louisiana, and Mississippi, it is. And as the map is put together by the compounding industry itself shows, there is a very large gray area in-between.

So why are we looking for anybody to blame other than the company and making sure that the regulators have all of the power that they need. That involves, my colleagues, regulatory power to act. It also involves, I tell you regulators, to do your action, to take action to stop these bad actors from doing what they want.

And I wasn't in the room, but I understand the chairman of the Oversight Committee said, they are not going to do any legislation.

Well, I would rather we do it now before he leaves. Because he is so involved and steeped in this whole question, he should want to work with us to solve this problem. It doesn't sound like that difficult a problem. We need to say the FDA has the authority to do this, to do this, to do that.

Commissioner Hamburg, can I ask you for a commitment to make your staff available to us this week if we started a process to——

Ms. HAMBURG. Absolutely, tomorrow. We are so eager to work with you because we feel there are significant gaps in our authorities that limit and undermine our ability to do all that we want to do to protect the health and safety of the American people. You know, I think that the fact that we have a situation like that map reveals, suggests that we don't have a comprehensive, integrated legal framework for action, and we think that we can work with you to identify critical areas from registration, so we know who is out there, and what they are doing, to developing Federal standards that should be adhered to to ensure safe and high-quality products, to the ability to do full inspections.

Mr. WAXMAN. I don't want to get you off the hook completely. I think you need the law to be clarified, but if I were sitting in your shoes—that is a mixed metaphor—if I were sitting in your seat and I was the head of the FDA and I heard that Colorado was concerned about this situation, and you heard other reports, I would have assumed I had jurisdiction. I would have assumed the jurisdiction. I would have acted on it.

And I have to say to the State, you know, people want to make partisan comments, and I think what some of what is going on is a little partisan. When FDA first sent the letter, the chairman said when you sent a letter, was the FDA under the Bush administration? When the State of Massachusetts had a weak consent agreement, it was under Governor Romney's administration. You are now here under Governor Deval Patrick and here under President Obama. Let's put partisanship aside. Let's make sure you have the authority and the resources to do the job. We want you to do the job because we ought to be mindful of the comments that Mrs. Lovelace made and all of the other people who are waiting to see if they are going to die from this contaminated drug.

We don't want excuses. We don't want to leave this law ambiguous because you are sued if you act. And if you act, assuming you have authority when you don't, you are usually called before committees to say, how could you act as if you have authority when Congress didn't give it to you?

I think we ought to put our partisanship aside. The election is over. Figure out a clear law for the Federal Government to be able to act because, because with all due respect, this is not a State issue if a drug is being shipped around in the country. It is an interstate issue.

Thank you, Mr. Chairman.

Mr. STEARNS. Sure, and I will be the first to recognize— to recommend you as you as chairman of the FDA.

Ms. DEGETTE. Can we finish this hearing, please?

Ms. HAMBURG. Might not want that job.

Mr. STEARNS. All right, Dr. Burgess is recognized.

Mr. BURGESS. Thank you, Mr. Chairman.

And something that is very important, I don't want it to get lost in the translation. Representative Blackburn asked about emails between the FDA regional office, and the Massachusetts Board of Pharmacy.

And Mr. Chairman, may I suggest that those emails are a critical part of our investigation and that we must receive those, even if it is necessary to exercise subpoena authority. We need access to that critical part of the——

Mr. STEARNS. If the gentleman will yield for one second. We have tried. We have got no emails from the FDA. The crux of this hearing is to get to the bottom of what happened. We can't get to the bottom if we don't have the information. So you are exactly right. The FDA has got to cooperate and give us the emails, because we have gotten zero.

Mr. BURGESS. Well, and of course, the FDA has a lot of material, and the access to the opinion of your experts would be important to us in this investigation. So the intransigence that Chairman Upton referenced in his opening statement is something that really must be overcome. Now, I am of the opinion that you had all of the authority that you needed, and yes, it was a previous commissioner, and it was a previous administration. So, once again, I would also ask that if there is a memo from a general counsel at FDA to the then commissioner about, you don't have the authority to do what you said you were going to do in this enforcement letter, I think the committee really should see that as well. And again, I think we should exercise every power that we have in order to get that. And the reason it is important is if new legislation is indeed passed and passed hurriedly, as has been recommended, before the end of the year, and yet you are not going to act on that authority, then we are going to be right back here in the same soup with the same problem at some point in the future, and it may be a different commissioner from the FDA and they will say, well, there was an ambiguity. Look, there is no ambiguity. You have got a criminal investigation going on against NECC, is that not correct?

Ms. HAMBURG. There is a criminal investigation, yes.

Mr. BURGESS. So where is the ambiguity? If you have a criminal investigation, if you had all of the guys in FDA jackets seizing computers out of the compounder, where is the ambiguity?

Ms. HAMBURG. First, let me say, we are working to get you the emails that you want. We have been trying to develop documents and get them to you as swiftly as we can in light of everything that is going on. You know, I know it is not the answer that you want to hear, but I do think that there is clearly ambiguity and a lack of——

Mr. BURGESS. A criminal investigation, guys in FDA jackets seized the computers, did it on TV so everybody can see. That doesn't look ambiguous——

Ms. HAMBURG. No, but—the need for legislation. You know, I want to do everything to work with you and get you the information that you need, but I think we also do need to look forward and look at where are the gaps in authority.

I cannot speak to what was going on in the FDA during that period because, as has been noted, I wasn't there.

As I understand it, there were very intense discussions and conflicts about what were our authorities, what—there was ongoing litigation; what basis would we use for different regulatory actions that might be taken.

Mr. BURGESS. So help us here. If we are going to craft legislation rapidly before the end of the year, as has been suggested several times on the other side of the dais, how do we keep from making the same mistake again? Look, do you have the authority to conduct an investigation as to whether or not you have jurisdiction to conduct an investigation because that is what I have been hearing all day?

Ms. HAMBURG. We have authorities that have been consistently contested, have resulted in split court decisions, in a patchwork of regulatory legal oversight, and you know, that is part of what I think we can and should address together.

Mr. BURGESS. Yes. Look, people are dead. Doctors have administered medication that they thought was safe, and their patients have suffered. They have got to live with those consequences. The case we heard about today where the doctors in the intensive care unit at Vanderbilt Hospital didn't have a clue as to what was really the culprit in that gentlemen's illness. There is a lot of stuff here that, if there is a problem with the existing statute, it needs to be corrected. Then you owe us the ability to look at those internal documents and see what the discussion——

Ms. HAMBURG. And we will get that to you.

Mr. BURGESS. Well, it has been said time again, we have to do this before the end of the year, give us the stuff. Mr. Chairman, I am going to ask that we subpoena the stuff that we need, and do that forthwith. I mean, yes, I know it is holiday season and nobody wants to be working on this stuff, but we have got to do it. And if we rapidly produce legislation so that we can just say we have done something before the end of the year so we can all feel good about ourselves, again, we are going to be back here in the same mess, 2 years, 3 years, 4 years fill in the blank. If all you need for the cloak of invisibility is to say you have a compounding pharmacist, I mean, what is to stop Pfizer tomorrow from saying, oh, I am a compounding pharmacist. All of this stuff goes out the door and you can't stop me. You can't touch me because the Fifth Circuit or the Ninth Circuit or someone said, you can't touch me. That is nonsense. No one believes that that is the way it should be, and surely, you don't either.

Ms. HAMBURG. I do not. And that is why I really do feel this is an extraordinary opportunity for us to fix some of those problems that have really been present for now at least 15 years and have tragically resulted in incidents involving deaths, loss of vision, other injuries and harm from drugs that the patients thought would help them, not harm them. So I think we can strengthen——

Mr. BURGESS. Look, you owe us the information you have.

Ms. HAMBURG. And we will get that to you.

Mr. BURGESS. You have emails. You have experts under your control. If this is something that has been discussed internally, and there has been a conflict internally, let us be privy of that information so that when we try to craft the legislative fix, it is not an imperfect product. And you have got all of the authority you need

today to shut this place down, lock them up, and send them away for however long that anyone would care to think, for whatever reason, it didn't happen in 2002, 2004, 2006, 2008.

Mr. STEARNS. The gentleman's time has expired.

Mr. BURGESS. I yield back.

Mr. STEARNS. Mr. Dingell, before I recognize Mr. Dingell, Dr. Hamburg, we have gotten thousands and thousands of emails from Dr. Smith's agency, so the fact that you have got none—she has less resources than you do, yet they complied and have given us all of the information. So I just really urge you and your staff to comply.

Ms. HAMBURG. We will get that to you.

Mr. STEARNS. All right, Mr. Dingell is recognized for 5 minutes.

Mr. DINGELL. Mr. Chairman, thank you.

Dr. Smith, and commissioner, it is possible for the two of you to execute Memorandums of Understanding defining your respective jurisdiction, is it not?

Ms. HAMBURG. Yes.

Mr. DINGELL. Is there any reason why you could not or would not begin to devote your attention to achieving such a Memorandum of Understanding so that you could define where the authorities of Food and Drug lie, and the authorities of the agency in the State of Massachusetts lie? Are you willing to undertake that, ladies?

Ms. SMITH. Well, I certainly think that there are multiple opportunities for us to do better in terms of communication and that sort of thing as a beginning.

Mr. DINGELL. We are going to try, I think you can sense from the committee and its questions to proceed towards a legislative solution, and it may very well be that we have to do so, and I think we are determined to do so.

What I am hoping is that while we are doing that, that you will commence doing what you have the capacity to doing, i.e. A Memorandum of Understanding, where the two of you define your respective responsibilities so that we can get ahead of this curve. And if we cannot complete our business by year end because of the Senate or other things, that we are able, therefore, because of your labors, to commence the process of moving along on a parallel track. Are you willing to do that?

Ms. HAMBURG. We are certainly willing to do that, and we are pulling together all of the 50 States in order to really begin——

Mr. DINGELL. Well, I don't want to put out difficulty for you, but I want to look at how to resolve the problem.

Ms. HAMBURG. But I just have to underscore that it still won't address what the courts say, different regulatory requirements.

Mr. DINGELL. Doctor, the clock runs, and it is most uncharitable.

I will look for you to give me an answer on what you can do to get a Memorandum of Understanding done between your two agencies and/or other agencies.

Now, it is possible to define a compounder as a person who makes certain amounts and to define a manufacturer as a person who makes certain amounts of pharmaceuticals, is it not? Yes or no?

Ms. HAMBURG. You could decide to put that in legislation. Currently, that does not exist in the legislation.

Mr. DINGELL. You are telling me you don't have the authority to do that? You do or don't have that authority?

Ms. HAMBURG. Volume in and of itself is not dispositive. It could be put into legislation as a statutory factor in our determination.

Mr. DINGELL. It appears that the New England Compounding Center and other like-hearted rascals have engaged in the practice of figuring themselves a fine loophole in which, through lobbying and other efforts, they have been able to assure that they are able to engage in practices that impose substantial dangers on the American people.

Now, having said that, I would like to have you tell me one more thing here, if you please, Doctor.

You have one of the required treatments for this particular fungicidal meningitis that takes place is to have availability of a substance called oral voriconazole, which is a therapy used in treating spinal meningitis. There is a great concern on the part of a hospital in my district St. Joseph Mercy in Ann Arbor, and they are troubled that there is going to be a shortage of this particular pharmaceutical available to them to provide the necessary treatments for their patients who have been hurt by this particular—the particular injectable that we are talking about today.

What is there that we can do to assure that there is an adequate, current, and future supply chain for oral voriconazole?

Ms. HAMBURG. Well, voriconazole has been used in the treatment intravenously, and from the very beginning, we have been looking at the possibility of shortages. When last I discussed that with——

Mr. DINGELL. What are we going to do about that?

Ms. HAMBURG [continuing]. They did not feel it was in shortage. I have not heard anything further. I will get back to you if there are concerns, but I do not believe that it is at risk for shortage at the present time.

Mr. DINGELL. This is a matter of urgent concern, and I would suspect that my people at St. Joe's are concerned that you all have hospitals and practitioners elsewhere in the country who all have the same concern. So I would appreciate if you can look——

Ms. HAMBURG. Yes, we will be examining that.

Mr. DINGELL [continuing]. Into that.

Mr. Chairman, I thank you for your courtesy.

Mr. STEARNS. The gentleman from Virginia is recognized for 5 minutes, Mr. Griffith.

Mr. GRIFFITH. Mr. Chairman, this is probably a first for me in the time that I have served on this committee, but I agree with Mr. Waxman when he said that he would have made the assumption, particularly in those areas that are gray, that you had the authority. And so I just point that out to you.

Now, maybe it is because I was a criminal defense attorney in my prior life, you know, the threats that somebody might sue me just aren't something that would stop me from trying to do my job. And if I thought I was right, I would have gone forward. And that is why we want to see the emails, and we want to see the memorandums. You have heard all of these questions, and I thought Ms. DeGette did a nice summation. And I wish you would have been as clear in your answers as she was in trying to interpret your position.

But having been a criminal defense attorney and having heard you all day say that, you know, you didn't have authority or your authority was vague, or you needed clarification of authority, I have to ask the question, what is your legal basis for the FDA going in and doing a criminal investigation in this case?

Ms. HAMBURG. Well, of course, that is being done with the Department of Justice, but the Food, Drug, and Cosmetics Act, obviously, is the basis for so much of our regulatory actions, but the problem here is that a component of 503(a) has been questioned in the courts, and it applies in some areas and it doesn't apply in other areas. And we have, around compounding pharmacies, we have guidance that we have put out that would be applying in some areas, but that doesn't have the force of law. So, you know, it is a challenging arena for regulatory——

Mr. GRIFFITH. Well, here is the problem, and I fear that in your comments today, you may have made the argument for the defense that they are going to escape criminal sanctions because you have said the law is ambiguous and that you don't have the authority to go forward. And I think that is a mistake because, look, you know, I think, as I said before, they are a manufacturer, particularly when we have 1,415 patients in my area alone. I think they are a manufacturer. And just because they call themselves a compounder doesn't make it so. I could call myself the Duke of Earl and claim diplomatic immunity. That does not make it so. In a trier of fact, if you all had been aggressive on this, I believe a trier of fact would have found they were weren't a compounder a long time ago, which is why, as you move forward, you didn't answer the question earlier, so I am assuming that you don't routinely contact medical professionals and ask them where they are getting their drugs from so that you couldn't identify. I think that is what you should have been doing, but hindsight is 20/20, as we all know.

But I think you ought to be looking at doing something like that in the future so that you can protect the American public. I think, like Mr. Waxman said, you should have assumed you had the authority when you had a bad actor. And I think as you go forward, you have to look at that. And Dr. Smith, I would hope that you all would look—I believe they may have undermined their criminal case today. So since they said it was a State's responsibility, perhaps there is a State law that you could look into and ask your attorney generals to look and see if there is any criminal prosecution that could be brought under State law, because if FDA doesn't have the authority to deal with them from a regulatory standpoint, I am not sure they have the authority to go in and seize the computers and do what they are doing.

That being said, I would now yield my time to the gentlewoman, Congresswoman Blackburn.

Mrs. BLACKBURN. Thank you. I appreciate that, and Dr. Hamburg, I want to go back to this issue with the emails that pertain to NECC. The first violation came up in 2002, and please understand that it was unclear in your answer to me about the emails. You seemed to indicate you thought we had your emails. We do not. So let me be very clear: We want to see this entire file going back to 2002. We want all of those emails, and we want the con-

versation that took place via email with the Massachusetts Board of Pharmacy.

I have 81 Tennesseeans and 13 deaths. We are very concerned about this. We are concerned about everyone that has been adversely impacted. Our sympathies and thoughts are with them, and we are incredibly concerned about the ineffectiveness of the bureaucracy, and it doesn't matter which administration. It is the lack of attention by this agency to a situation that has gotten out of hand.

So just to be certain that you understand what we are asking, all of the emails, we are not in possession of this. We are—and we have asked for this. So we do ask that you comply quickly, so that we can see the full extent to your participation and the manner in which you all communicated with, responded both on an intra-agency, and then also with the Massachusetts Board of Pharmacy.

And with that, I will yield back the balance of my time.

Mr. STEARNS. The gentlelady's time—gives up her time, and the gentleman from Massachusetts is recognized for 5 minutes.

Mr. MARKEY. Thank you, Mr. Chairman, very much.

Dr. Hamburg, isn't it true that the legal definition of drug manufacturer in Section 510 of the Food, Drug, and Cosmetics Act exempts pharmacies?

Ms. HAMBURG. You know, I am not a lawyer, but my understanding is yes.

Mr. MARKEY. Yes. So that creates a problem right up front from a legal perspective.

Ms. HAMBURG. Yes.

Mr. MARKEY. That clear statement that exempts pharmacies from FDA jurisdiction, and when it comes to drug manufacturers, that in the actual definition itself, it kind of talks about what would be equivalent of Merck, Bayer, or Pfizer as a manufacturer, and then it explicitly says pharmacies aren't covered, you know, in that definition. So that is just loaded with potential for lawsuits, you know, for questions that can be raised about your authority, and do you need that clarified so that you absolutely have the ability to regulate compounding pharmacies in a way that protects the public health and safety?

Ms. HAMBURG. I think that 510 exempts from registration, not any kind of jurisdiction, but I think the problem is that—I am not saying we have no authority. I am saying that our authority over drug manufacturers is very different, and it requires a set of clear actions on the part of the manufacturers and the part of FDA.

In this area, it is simply much more murky, and it is contested in the courts, and we have a split court decision. We have different legal frameworks that govern different States, yet we have an industry that operates across State boundaries.

We don't have the kind of authorities that we need, and we don't have the kind of clarity of the legislation that we need as well, you know. I am deeply troubled by what has happened in this case and with NECC, and if there were actions that could have been taken at an earlier time to prevent it, I would wish that that were so.

But you know, what I am speaking to now is, we have this opportunity. It is a clarion call to action, I think. And if we don't want to see that kind of event repeated, and it is not an event that has

occurred in isolation, you know. There have been events in so many Members' districts in the past over a period of many years, that I think we have an obligation to work together to create new legislation that defines this in a way that is clear and understood and that gives FDA new authorities.

Mr. Griffith mentioned, you know, why aren't we writing to compounders, or why aren't you writing to patients telling them that they might be getting drugs from compounders? Well, we don't even know the universe of compounders and what they are making. So we clearly need additional authorities in order to achieve some of this goals that we have been talking about.

Mr. MARKEY. And, Doctor, that is why I listed the individual component parts of my legislation, just so it could be clear that you would welcome that authority. And then we could ensure that you can be the true cop on the beat.

But I do believe that it is troublesome that in the legal definition of "drug manufacturer," the legal definition in the FDA statute, it actually exempts pharmacies in that definition.

So the whole area is just rife with ambiguity. And in that atmosphere of ambiguity, we have wound up with a mess on our hands. And we just have to make sure that that never happens again.

Mr. Chairman, I thank you so much.

Mr. STEARNS. Thank you.

And I would say to the panel, we have completed our questions here. And, as the chairman, I have usually the ability to say the last few words. And in defense of Mr. Markey, who had made the case, in his words, as murky, I go back to what Mr. Waxman said, that if he was chairman of the FDA, he would not have been cautious; he would have been siding on safety and gone through and exercised, regardless of what the situation. I agree with him, and that is why I think he probably should consider being the commission chairman.

And, also, I would say to you, if Pfizer or Merck or any large pharmaceutical company suddenly call themselves a compounding company, you are implying that you wouldn't have jurisdiction over them, when we know that is not true. In fact, you know, when you look historically, you see lots of criminals that are being indicted; they make the case that, "I was doing work for the FBI under cover." And, lo and behold, that was just a front so that they could defend themselves when, actually, they were committing fraud and criminal activity.

And, lastly, I would just conclude, Mr. Griffith and Dr. Burgess both mentioned the FDA appears to have the legal authority to walk in and take computers with their jackets, we have seen on television. And, certainly, if you had the ability to go in and prosecute and take the computers from NECC, then surely you had the jurisdiction to shut them down, because you had the jurisdiction to go in and take their equipment.

And, certainly, I think many of us in this committee are disappointed that you are not providing the emails and information we need so we can get to the bottom of this. And that was the intention of this whole hearing, is to see what really happened.

So, with that, the subcommittee is adjourned.
[Whereupon, at 2:00 p.m., the subcommittee was adjourned.]
[Material submitted for inclusion in the record follows:]

Terry Opening Statement for the Fungal Meningitis Outbreak Hearing

WASHINGTON, DC – Congressman Lee Terry (R-NE) issued the following statement today:

"Mr. Chairman: Thank you for allowing me to submit this statement for the record. I sit here today as a very concerned Member of this Oversight panel. How is it that after nearly a decade of documented evidence against a 'bad player' the FDA failed to act? Even after a letter in 2006 that threatened enforcement action?

"The issue at hand here is not whether FDA lacks the authority. It is clear that their authority was enforced when they raided the NECC this year. My worry is that the FDA may lack the leadership necessary to see these kinds of problems coming. How is it possible that in the three weeks between September 25, 2012 and October 16, 2012, more damming information was gleaned than what was gleaned over nearly a decade of documented violations by the NECC from 2003-2012? Does it take people dying for FDA to act?

"I look forward to today's testimonies."

The House Committee on Energy and Commerce

November 14, 2012

The Fungal Meningitis Outbreak: Could It Have Been Prevented?

Document Binder

Committee on Energy and Commerce
Subcommittee on Oversight and Investigations

United States House of Representatives
Committee on Energy and Commerce
Subcommittee on Oversight and Investigations
"The Fungal Meningitis Outbreak: Could It Have Been Prevented?"
November 14, 2012 10:00 AM
Rayburn House Office Building Room 2123

Exhibit List

1. MASS. DEP'T OF PUB. HEALTH, NEW ENGLAND COMPOUNDING CENTER (NECC) PRELIMINARY INVESTIGATION FINDINGS: BD. OF REGISTRATION IN PHARMACY REPORT (Oct. 23, 2012).

2. U.S. FOOD & DRUG ADMIN., NEW ENGLAND COMPOUNDING CENTER FORM FDA 483 (Oct. 26, 2012).

3. Advisory Letter from James T. Devita, President, Mass. Bd. of Registration in Pharmacy, to Barry Cadden, Manager of Record, New England Compounding Ctr. (Sept. 30, 2004) (Docket Nos. DS-03-060, PH-03-070 – Texas).

   Advisory Letter from James T. Devita, President, Mass. Bd. of Registration in Pharmacy, to Barry Cadden, Manager of Record, New England Compounding Ctr. (Sept. 30, 2004) (Docket Nos. DS-04-062, PH-04-161 – Iowa and Wisconsin).

   Advisory Letter from James T. Devita, President, Mass. Bd. of Registration in Pharmacy, to Barry Cadden, Manager of Record, New England Compounding Ctr. (Sept. 30, 2004) (Docket Nos. DS-03-036, PH-03-042 – South Dakota).

4. U.S. FOOD & DRUG ADMIN., NEW ENGLAND COMPOUNDING PHARMACY, INC. FORM FDA 483 (Apr. 16, 2002).

   U.S. FOOD & DRUG ADMIN., FDA INSPECTION REPORT OF NEW ENGLAND COMPOUNDING PHARMACY, INC. (Apr. 16, 2002).

5. MASS. DEP'T OF PUB. HEALTH, INVESTIGATION REPORT OF NEW ENGLAND COMPOUNDING CENTER & BARRY CADDEN (Mar. 4, 2004).

6. U.S. FOOD & DRUG ADMIN., NEW ENGLAND COMPOUNDING CENTER FORM FDA 483 (Feb. 10, 2003).

   U.S. FOOD & DRUG ADMIN., FDA ESTABLISHMENT INSPECTION REPORT OF NEW ENGLAND COMPOUNDING CENTER (Feb. 10, 2003).

   U.S. FOOD & DRUG ADMIN., FDA INSPECTION REPORT OF NEW ENGLAND COMPOUNDING CENTER (Feb. 10, 2003).

7. Memorandum from Consumer Safety Officer, New England Dist. Office, FDA & Compliance Officer, New England Dist. Office, FDA, to Central File, *February 5, 2003 Meeting with Massachusetts Board of Pharmacy/Division of Professional Licensure (239 Causeway Street, Boston, MA 02114)* (Feb. 24, 2003).

8. Letter from Charles R. Young, Executive Dir., Mass. Bd. of Registration in Pharmacy, to Barry J. Cadden, Manager of Record, New England Compounding Ctr. (Oct. 4, 2004).

   Proposed Consent Agreement, *In the Matter of New England Compounding Center Registration No. 2848 Barry J. Cadden, R.Ph. License No. 21239*, Docket Nos. DS-03-055, PH-03-066 (Mass. Bd. of Registration in Pharmacy, Oct. 4, 2004).

9. Letter from Paul R. Cirel, Counsel to Barry Cadden & New England Compounding Ctr., to Susan Manning, Counsel to Mass. Bd. of Registration in Pharmacy (Nov. 11, 2004).

10. Memorandum from Investigator, New England Dist. Office, FDA, to Acting Team Leader, Div. of New Drugs & Labeling Compliance, FDA, *Inspection/Investigation of New England Compounding Center 697 Waverly Street Framingham, MA 01702* (Jan. 26, 2005).

11. MASS. DEP'T OF PUB. HEALTH, INVESTIGATION REPORT OF BARRY CADDEN (Nov. 23, 2004).

12. Consent Agreement, *In the Matter of New England Compounding Center Registration No. 2848 Barry J. Cadden, R.Ph. License No. 21239*, Docket Nos. DS-03-055, PH-03-066, DS-05-040 (Mass. Bd. of Registration in Pharmacy, Jan. 10, 2006).

13. Warning Letter (NEW-06-07W) from Gail T. Costello, Dist. Dir., New England Dist. Office, FDA, to Barry J. Cadden, Dir. of Pharmacy, New England Compounding Center (Dec. 4, 2006).

14. Letter from Barry J. Cadden, Dir. of Pharmacy, New England Compounding Center, to Compliance Officer, New England Dist. Office, FDA et al. (Jan. 5, 2007).

15. Letter from Compliance Officer, New England Dist. Office, FDA, to Barry J. Cadden, Dir. of Pharmacy, New England Compounding Center (Oct. 31, 2008).

16. Cease and Desist Order, *In the Matter of the Unauthorized and Unlawful Distribution of Prescription Drugs and/or Compounded Prescription Drugs in Colorado by New England Compounding Center, Inc.*, Case No. 2011-3973 (Colo. State Bd. of Pharmacy, Apr. 15, 2011).

17. E-mail from Pharmacy Inspector, Colo. State Bd. of Pharmacy, to James D. Coffey, Dir., Mass. Bd. of Registration in Pharmacy (July 26, 2012, 3:06 PM).

E-mail from James D. Coffey, Dir., Mass. Bd. of Registration in Pharmacy, to Pharmacy Inspector, Colo. State Bd. of Pharmacy (July 27, 2012, 7:33 AM).

E-mail from James D. Coffey, Dir., Mass. Bd. of Registration in Pharmacy, to Susan Manning, Counsel to Mass. Bd. of Registration in Pharmacy et al. (July 27, 2012, 7:34 AM).

18. E-mail from Senior Case Review Expert, Denver Dist. Office, FDA, to Supervising Consumer Safety Officer, New England Dist. Office, FDA et al. (May 10, 2011, 4:19 PM).

19. Press Release, Mass. Dep't of Pub. Health, Statement of Interim Commissioner Dr. Lauren Smith on NECC Investigation (Nov. 7, 2012).

20. E-mail from Charles R. Young, Executive Dir., Mass. Bd. of Registration in Pharmacy, to Jean Pontikas, Dir., Div. of Health Professions Licensure et al. (Nov. 15, 2004, 1:07 PM).

21. E-mail from Prosecuting Counsel, Office of Gen. Counsel, Mass. Dep't of Pub. Health, to Charles R. Young, Executive Dir., Mass. Bd. of Registration in Pharmacy (Oct. 27, 2005, 9:04 AM).

22. E-mail from Charles R. Young, Executive Dir., Mass. Bd. of Registration in Pharmacy, to Prosecuting Counsel, Office of Gen. Counsel, Mass. Dep't of Pub. Health et al. (Nov. 18, 2005, 9:41 AM).

23. E-mail from Prosecuting Counsel, Office of Gen. Counsel, Mass. Dep't of Pub. Health, to Charles R. Young, Executive Dir., Mass. Bd. of Registration in Pharmacy et al. (Dec. 2, 2005).

24. E-mail from Charles R. Young, Executive Dir., Mass. Bd. of Registration in Pharmacy, to Risk Manager, Brigham & Women's Hosp. et al. (Sept. 16. 2005, 8:23 AM).

25. E-mail from Susan Manning, Counsel to the Mass. Bd. of Registration in Pharmacy, to Jean Pontikas, Dir., Div. of Health Professions Licensure et al. (Apr. 24, 2006).

THE COMMONWEALTH OF MASSACHUSETTS
EXECUTIVE OFFICE OF HEALTH AND HUMAN SERVICES
Massachusetts Department of Public Health

New England Compounding Center (NECC)

Preliminary Investigation Findings

BOARD OF REGISTRATION IN PHARMACY REPORT

October 23, 2012

THE COMMONWEALTH OF MASSACHUSETTS
EXECUTIVE OFFICE OF HEALTH AND HUMAN SERVICES
DEPARTMENT OF PUBLIC HEALTH
PRELIMINARY INVESTIGATION REPORT – NECC 2012

INTRODUCTION

Since September 24, 2012 a widespread outbreak of fungal meningitis has affected people in 17 states and caused 23 deaths at the time of this report. The outbreak originated from a medication compounded by New England Compounding Center (NECC), a facility licensed by the Massachusetts Board of Registration in Pharmacy (Board). The Massachusetts Department of Public Health (DPH) has taken immediate action to protect public health and safety. In collaboration with investigators from the U.S. Food and Drug Administration (FDA), DPH investigators have worked to identify the root causes of these events. While the complete scope and severity of this outbreak will not be fully understood for many weeks, to ensure the utmost transparency, DPH is releasing these preliminary findings from its ongoing investigation of NECC. This report constitutes early findings that may be subject to revision as the investigation unfolds.

Medication compounding involves the practice of taking commercially available products and modifying them to meet the needs of an individual patient pursuant to a prescription from a licensed provider. Nearly all retail pharmacies in Massachusetts perform compounding, however only 25 compounding pharmacies meet the standards necessary to produce sterile injectable products. By terms of their license with the Board, every Massachusetts pharmacy must comply with Massachusetts laws and regulations, including compliance with the United States Pharmacopeia Standards. Compounding pharmacies may only perform compounding upon receipt of a patient-specific prescription. These requirements and restrictions are consistent with the rules in place in other states.

Upon beginning the joint on-site investigation of NECC early in this outbreak, DPH and FDA investigators identified serious deficiencies and significant violations of pharmacy law and regulations that clearly placed the public's health and safety at risk.

KEY FACTS

DATE(S) OF INVESTIGATION: *September 26, 2012 to Present*
PHARMACY LICENSE NUMBER AND INITIAL ISSUE DATE: *DS2848; July 16, 1998*
LICENSE STATUS: *Voluntary Surrender, October 3, 2012*
CORPORATION NAME: *New England Compounding Pharmacy, Inc.*
DBA NAME: *New England Compounding Center (NECC)*
ADDRESS: *697 Waverly Road, Framingham, MA, 01702*
MANAGER OF RECORD AND LICENSE NUMBER: *Cadden, Barry J; PH21239*
DEA REGISTRATION NUMBER AND EXPIRATION DATE: *BNS927819, July 31, 2013*
PRACTICE SETTING: *Specialty Pharmacy*
PREVIOUS INSPECTION DATE: *May 24, 2011*
PREVIOUS INSPECTION DOCKET OR STAFF ASSIGNMENT NUMBER: *ISP-738*

INVESTIGATIVE METHODOLOGY

The NECC on-site investigation process consisted of DPH investigators obtaining documentary evidence (including photographs), reviewing and obtaining copies of Standard Operating Procedures, observational findings, reviewing and obtaining copies of all policies and procedures, reviewing batch records and interviewing NECC staff. The FDA conducted product testing and investigators took environmental samples of various areas of the facility to test for contaminants.

DPH investigators principally communicated with three NECC staff members during the on-site investigation (Barry J. Cadden, Glenn A. Chin and Lisa Conigliaro-Cadden) along with FDA investigators. After September 26, 2012, the majority of NECC employees were no longer on site. As has publicly been documented, NECC terminated many of their staff. The continuing investigation will include interviews of NECC employees.

SELECTED PRELIMINARY FINDINGS

During the facility inspections, investigators documented serious health and safety deficiencies related to the practice of pharmacy. All pertain to violations of 247 CMR 9.01(3) or 247 CMR 6.01(5)(a):

- NECC distributed large batches of compounded sterile products directly to facilities apparently for general use rather than requiring a prescription for an individual patient.
    - Records show that NECC had lists of potential patient names but did not have patient-specific prescriptions from an authorized practitioner when compounding and dispensing medication, as required by state law.
    - Manufacturing and distributing sterile products in bulk was not allowed under the terms of its state pharmacy license. If NECC was appropriately licensed as a manufacturer with the FDA the company would have been subject to additional levels of scrutiny.
    - NECC did not conduct patient-specific medication history and drug utilization reviews as required by regulations.

- NECC distributed two of the recalled lots of methylprednisolone acetate (PF) 80 MG/ML prior to receiving results of sterility testing:
  - Lot *06292012@26* was prepared on June 29, 2012. Final sterility testing was completed on July 17, 2012. Two shipments of product were made prior to the final sterility tests results being received.
  - Lot *08102012@51* was prepared on August 10, 2012. Final sterility testing was completed on August 28, 2012. Eleven shipments of product were made prior to the final sterility tests results being received.
  - While NECC's records show the sterility tests found no contamination, the adequacy of NECC's sterility testing methods are currently under examination.
- Final sterilization of product did not follow proper standards for autoclaving (sterilization through high pressure steam) pursuant to United States Pharmacopeia Standard 797 (USP 797) and NECC's own Standard Operating Procedures:
  - Examination of NECC records indicated a systemic failure to keep products in the autoclave for the required minimum 20-minute sterilization period necessary to ensure product sterility.
- NECC did not conduct proper validation of autoclaves pursuant to USP 797:
  - NECC failed to test their autoclaves to ensure proper function.
- Visible black particulate matter was seen in several recalled sealed vials of methylprednisolone acetate from Lot *08102012@51*.
- Powder hoods, intended to protect pharmacists from inhaling substances during medication preparation, within the sterile compounding area were not thoroughly cleaned pursuant to USP 797.
  - Residual powder was visually observed within the hood during inspection. This contamination may subsequently lead to contamination of compounded medications.
- Condition of "Tacky" mats, which are used to trap dirt, dust, and other potential contaminants from shoes prior to clean room entry, violated the USP 797.
  - Mats were visibly soiled with assorted debris.

- A leaking boiler adjacent to the requisite clean room created an environment susceptible to contaminant growth:
  - A pool of water was visually observed around the boiler and adjacent walls, creating an unsanitary condition; the culture results of this potential contaminant are still pending.

CHRONOLOGY OF THE OUTBREAK & DEPARTMENT OF PUBLIC HEALTH ACTIONS

Monday September 24, 2012 – The Massachusetts Department of Public Health (DPH) was notified by Tennessee Department of Health in late evening about a cluster of six rare fungal meningitis cases, with onset of symptoms between July 30 and September 18, 2012. These patients had several risk factors in common, including an epidural injection of steroid (methylprednisolone acetate 80 mg/ml preservative free) compounded at New England Compounding Center (NECC) located in Framingham. Tennessee also reviewed three other products not made by NECC as potential contaminants.

Tuesday September 25, 2012 – DPH planned an investigation of NECC given growing concerns of linkage to infections. The DPH's Bureau of Health Care Safety and Quality, Board of Registration in Pharmacy (Board), and Bureau of Infectious Diseases began rapid response planning on September 25, and convened a multi-agency meeting between the Tennessee Department of Health, the U.S. Centers for Disease Control and Prevention (CDC), the U.S. Food and Drug Administration (FDA), and the New England Compounding Center (NECC). At the demand of DPH staff, Barry Cadden and Gregory Conigliaro, principal owners of NECC, immediately provided documentation of all facilities in the nation that had received medications from three lots of methylprednisolone acetate that were suspected by the CDC as being linked to the fungal infections ("suspect lots"). Distribution lists were provided to public health authorities across the country, including CDC and FDA. The suspected product was distributed to more than 14,000 patients in 23 states.

Suspect Lots of Methylprednisolone Acetate (PF) 80 mg/ml Injection identified by TN DOH:

Lot #05212012@68 prepared by NECC on 5/21/2012
Lot #06292012@26 prepared by NECC on 6/29/2012
Lot #08102012@51 prepared by NECC on 8/10/2012

17,676 total doses

Wednesday September 26, 2012 – DPH began an onsite investigation of NECC and instituted a recall of all suspect lots of methylprednisolone acetate. Investigators confirmed that all non-distributed methylprednisolone products were quarantined, and that methylprednisolone acetate was no longer being produced. Approximately 3,000 doses were quarantined or returned through recall. Upon arriving at NECC, investigators found NECC employees cleaning sterile compounding areas and conducting environmental testing. DPH investigators also detected signs of bleach decontamination in the compounding areas.

Thursday September 27, 2012 to Sunday September 30, 2012 – DPH coordinated with FDA to plan a collaborative investigation of NECC.

Monday October 1, 2012 – DPH and FDA began a joint investigation at NECC. Findings supported by the epidemiological work of the CDC prompted DPH to issue a formal Quarantine Notice pursuant to M.G.L. c. 94C, §§ 13 and 189A, and M.G.L. c. 112, §§ 30 and 42A. This legally formalized the September 26 quarantine action. The Notice directed that all methylprednisolone acetate raw materials (chemicals), all non-sterile and sterile products located at NECC used in the compounding of methylprednisolone acetate, and all inventory on the premises prepared for dispensing and stored at the pharmacy, or received by recall should be quarantined and not disposed of without the express approval of the DPH. Investigators were shown examples of methylprednisolone products that were labeled as patient specific. The associated documents were not individual prescriptions but lists of patients generated by a clinical facility and provided to NECC to obtain the product. NECC stated the list of names was considered to be an authorized prescription by the physician. This practice is not in accordance with Massachusetts regulations.

Tuesday October 2, 2012 – DPH and FDA observed visible black particulate matter in sealed vials (of purportedly sterile methylprednisolone acetate) returned to NECC. Inconsistencies in sterilization processes of materials were identified through review of NECC's records. The Board voted to obtain a Voluntary Surrender of NECC's license or to initiate action to issue a Temporary Order of Summary Suspension.

Wednesday October 3, 2012 – DPH secured voluntary surrender of NECC's license, effective 12 pm (noon), and instituted a voluntary recall of all intrathecal products (those injected into the area around

the spinal cord or brain). DPH also notified Massachusetts providers to cease use of all NECC products.

Thursday October 4, 2012 – DPH and FDA publicly announced that black particulate matter, tentatively identified by microscopy as fungal contamination, was seen in a sealed, purportedly sterile vial of methylprednisolone acetate from a suspect lot. CDC and FDA recommended that all health care professionals cease use and remove from their pharmaceutical inventory any material produced by NECC. Massachusetts State Epidemiologists contacted nine Massachusetts health care facilities that received non-implicated lots of methylprednisolone acetate, instructing them to contact recipient patients to determine whether there were any unusual infections or other complications. No infections from the non-implicated lots sent to Massachusetts facilities have been identified at this time. DPH and FDA investigators continued with their on-site investigation and evaluated standard operation procedures and batch records related to sterile compounding. FDA investigators took environmental samples of various areas of the facility to test for contaminants.

Friday October 5, 2012 – DPH and FDA investigators noted visible contaminants in additional sealed recalled vials of methylprednisolone acetate. The particulate matter was noted in vials labeled in conformance with Massachusetts pharmacy regulations with patient-specific information. Additionally, particulate matter was noted in recalled vials that were labeled without patient-specific names, in clear violation of Massachusetts regulations. DPH and FDA each issued an alert to providers and facilities across the country stating the identification of particulate matter.

Saturday October 6, 2012 – DPH secured an immediate recall of all NECC products.

Monday October 8, 2012 – At the request of DPH, Barry Cadden and Glenn Chin, leaders at NECC, voluntarily ceased practice as pharmacists pending completion of the investigation.

Wednesday October 10, 2012 – Based on their shared ownership and leadership with NECC, DPH requested that Ameridose and Alaunus Pharmaceutical cease all pharmacy operations and any dispensing, manufacturing or wholesale distribution of any products starting at 3 p.m. on October 10 and continuing until 5 p.m. on October 22. DPH and FDA staff began an on-site investigation of Ameridose, a pharmacy, distributor and wholesaler regulated by the FDA. At the demand of DPH, Barry J. Cadden agreed to immediately resign as manager, director and from any other management

position at NECC, Ameridose, and Alaunus. DPH began working with the Massachusetts Hospital Association to ensure that the supply chain of medications would not be disrupted. The Board issued an advisory to all pharmacies and pharmacists in Massachusetts emphasizing that all of their actions must be performed in accordance with the United States Pharmacopeia. The advisory also reiterated that state law requires compounding pharmacies and
pharmacists to have a patient-specific prescription from an authorized practitioner when compounding and dispensing medication. Compounding pharmacies and pharmacists were required to submit an affidavit asserting that they are following state law in this regard.

Sunday October 14, 2012 – DPH staff began on-site investigation of Alaunus Pharmaceuticals, a wholesale distributor affiliated with Ameridose and NECC.

Monday October 15, 2012 – FDA issued an advisory that a patient may have acquired fungal meningitis from a different NECC steroid injection, triamcinolone acetonide. DPH epidemiologists began outreach to all 192 facilities in Massachusetts who received any NECC injectable products and supported providers in patient outreach. In addition, the FDA reported a transplant patient with an *Aspergillus fumigatus* infection who received a NECC cardioplegic solution during surgery. The CDC is actively working to confirm the presence of fungal contaminants in cardioplegic solutions. DPH asked Massachusetts providers to contact any patients who received any injectable product, including ophthalmic drugs or cardioplegia solutions prepared by NECC after May 21, 2012.

Thursday October 18, 2012 – FDA released definitive laboratory confirmation of the presence of fungal contaminants in sealed vials of methylprednisolone acetate in a suspect lot prepared by NECCDPH and FDA collected samples from sealed vials of completed product at Ameridose. Results are currently pending with the FDA.

Friday October 19, 2012 – DPH and FDA investigators scrutinized business practices of Alaunus Pharmaceuticals, and potential for inappropriate distribution of NECC or Ameridose products. At the request of DPH, Ameridose and Alaunus Pharmaceuticals extended their cessation of operations until November 5, 2012.

Monday October 22, 2012 – The Board authorized DPH staff to request voluntary permanent surrender of the licenses of Barry J. Cadden, Glenn A. Chin, and Lisa Conigliaro-Cadden, as well as

NECC. If the three pharmacists and NECC do not comply, the Board authorized staff to proceed with permanent revocation. All three individuals are currently prevented from practicing as pharmacists, and would be so prohibited throughout the appeal process.

ONGOING INVESTIGATION

The Department's collaborative investigation with the FDA is comprehensive and will continue until investigators have all information needed to determine what, if any, further action should be taken against NECC and its leadership. This investigation also extends to NECC's business practices and environmental conditions surrounding the business, including the presence of a nearby recycling center that shares ownership with NECC. Investigators are also looking into NECC's corporate entity, including, but not limited to, corporate ownership and governance structures at both NECC and sister companies, Ameridose and Alaunus. DPH will analyze and incorporate all evidence and information gathered by the FDA and the Board of Registration in Pharmacy into a final, comprehensive report. This report will be presented to the Board of Registration in Pharmacy, which will determine appropriate regulatory sanctions under administrative law. DPH will also assist with any investigation, federal or state, that explores the actions of NECC and its principals. DPH will continue to support and cooperate with federal policymakers in addressing gaps in oversight of compounding pharmacies, including leaders on the U.S. Senate Health, Education, Labor, and Pensions Committee, and the U.S. House of Representatives Energy and Commerce Committee, and members of the Massachusetts Congressional delegation, including Congressman Ed Markey. DPH will also work closely with the Massachusetts General Court to explore state-specific policy solutions. Findings of these investigations will be used to inform these state and federal actions to address regulatory gaps within the quickly evolving compounding industry.

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT OFFICE ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
New England District Office 1 Montvale Ave, Stoneham, MA 02180	10/1-2, 10/4-5, 10/9, 10/15, and 10/26/12
[redacted] Industry Information: www.fda.gov/oc/industry	FEI NUMBER 3003623877

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: Barry J. Cadden, Owner

FIRM NAME	STREET ADDRESS
New England Compounding Pharmacy Inc., d/b/a New England Compounding Center	697 Waverly Street
CITY, STATE AND ZIP CODE	TYPE OF ESTABLISHMENT INSPECTED
Framingham, MA 01702	Compounding Pharmacy

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DURING AN INSPECTION OF YOUR FIRM WE OBSERVED:

1. On 10/02/2012, we observed approximately eighty-three (83) vials out of a bin containing 321 vials of methylprednisolone acetate (preservative free) 80mg/mL from Lot #08102012@51 (shipped to customers between 8/17/12 – 9/25/12 per firm distribution data), a sterile injectable drug, to contain what appeared to be greenish black foreign matter. Seventeen (17) vials from the same bin of methylprednisolone acetate (preservative free) 80mg/mL were observed to contain what appeared to be white filamentous material.

The sterility sample taken by the firm consisting of one 5ml vial of bulk formulated methylprednisolone acetate (preservative free) from lot 08102012@51 resulted in a sterile result (lab analysis started 8/14/12 and reported 8/28/12). However, the FDA analysis of FDA Sample #693965, consisting of methylprednisolone acetate (preservative free) 80mg/mL, 1mL filled vials, from Lot #08102012@51 collected from the firm, confirmed the presence of viable microbial growth in 50/50 vials tested. One vial examined microscopically showed fungal morphological features.

2. Although the formula worksheets state the raw materials are sterile, the Pharmacy Director stated that the firm uses non sterile active pharmaceutical ingredients (APIs) and raw materials, with the exception of sterile water for injection, to formulate injectable suspensions including but not limited to preservative free methylprednisolone acetate and triamcinolone. During the inspection, we observed that the labeling for the methylprednisolone API and additional raw materials did not indicate that they were sterile. Samples were collected for analysis of the non-sterile API and 3 additional raw materials used in the formulation of methylprednisolone acetate. The firm provided no documentation or evidence to support that the steam autoclave cycle used to sterilize suspensions formulated using non-sterile API and raw materials is effective.

3. The firm's environmental monitoring program yielded the following microbial isolates (bacteria and mold) within Clean Room 1 and Clean Room 2, used for the production of sterile drug products, between January 2012 and September 2012. Firm personnel stated that the firm shuts off the air conditioning from 8:00 pm to 5:30 am nightly in the Clean Room.

Table #1: Surface Samples from ISO 6 (Class 1,000) Rooms
Alert: 3 CFU Action: 5+ CFU

Location	Result Bacteria	Result Mold	Date
Main Clean Room	[redacted]		
CRBin1 (polymyxin under station 1)	0	1	2/16/12
4 FLR (near hood 5)	10*	2*	2/23/12
2 FLR (near hood 3)	3	1	3/8/12

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[redacted]

DATE ISSUED

10/15

FORM FDA 4[redacted] INSPECTIONAL OBSERVATIONS Page 1 of 8

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT OFFICE ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
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DURING AN INSPECTION OF YOUR FIRM WE OBSERVED:

Location	Result Bacteria	Result Mold	Date
4 FLR (near hood 5)	2	2	3/15/12
Table 2	0	1 mold (¾ of plate)*	3/29/12
1 FLR (near hood 1)	One hair with growth around it		3/29/12
4 FLR (near hood 5)	OG*	0	4/5/12
CRBin1 (inside big uline bin with omnipaque 240)	1	1	6/13/12
3 FLR (near horiz hoods)	OG*	0	6/13/12
3 FLR (near horiz hoods)	1	2	6/28/12
CRBin2 (front of tetracaine Hcl powder container)	0	OG mold*	7/5/12
Pass thru	0	1 small mold	7/26/12

Note: (*) indicates result over action level; OG indicates over growth

Table #2: Surface Samples of ISO 7 (Class 10,000) Rooms
Alert: 5 CFU Action: 7+ CFU

Location	Result Bacteria	Result Mold	Date
Gown Room (Clean Room 1)	[redacted]		
8 FLR (GR/near hooks)	23*	0	2/16/12
GRmisc2 (vent arms)	13*	1*	2/16/12
GRmisc2 (empty plastic bag in empty bin)	19*	0	2/23/12
GRmisc1 (vent arms behind hand washer)	27*	0	2/23/12
7 FLR (gown room/entrance)	2*	11*	2/23/12
8 FLR (gown room/near hooks)	11*	4*	2/23/12
7 FLR (gown room/entrance)	0	1	3/1/12
WallGR2 (windowsill side to MR)	18*	0	3/1/12
8 FLR (gown room/near hooks)	12*	0	3/1/12
GRmisc2 (vent grids)	16*	2*	3/1/12
7 FLR (gown room/entrance)	3	2	3/8/12
8 FLR (gown room/near hooks)	3	2	3/8/12
7 FLR (gown room/entrance)	3	3	3/15/12
8 FLR (gown room/near hooks)	0	2	3/15/12
8 FLR (gown room/near hooks)	16*	0	3/29/12

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DATE ISSUED 10/31/12

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT OFFICE ADDRESS AND PHONE NUMBER
New England District Office 1 Montvale Ave, Stoneham, MA 02180

DATE(S) OF INSPECTION
10/1-2, 10/4-5, 10/9, 10/15, and 10/26/12

[redacted] Industry Information: www.fda.gov/oc/industry

FEI NUMBER
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TO: Barry J. Cadden, Owner

FIRM NAME
New England Compounding Pharmacy Inc., d/b/a New England Compounding Center

STREET ADDRESS
697 Waverly Street

CITY, STATE AND ZIP CODE
Framingham, MA 01702

TYPE OF ESTABLISHMENT INSPECTED
Compounding Pharmacy

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DURING AN INSPECTION OF YOUR FIRM WE OBSERVED:

Location	Result Bacteria	Result Mold	Date
GRmisc2 (floor under barrel against wall)	11*	0	3/29/12
8 FLR (gown room/near hooks)	10*	0	4/5/12
7 FLR (gown room/entrance)	0	1	4/5/12
GRmisc1 (rubber flap over wheel of rack)	9*	0	4/12/12
WallGR1 (window sill side to middle room)	9*	0	4/12/12
GRmisc1 (top of rack with bouffants)	12*	0	5/10/12
7 FLR (GR/entrance)	2	1	5/31/12
8 FLR (GR/near hooks)	19*	0	5/31/12
8 FLR (GR/near hooks)	0	13*	6/28/12
7 FLR (GR entrance)	3	3	6/28/12
GRmisc1 (bottom of bootie bin)	¾ of plate OG*	1*	7/26/12
GRmisc2 (bottom of mask bin)	plate ¾ overgrown*	0	7/26/12
8 FLR (GR/near hooks)	9*	0	7/26/12
GRmisc2 (front of 7-7.7 glove bin)	OG*	1*	8/2/12
GRmisc2 (loose bootie bin)	0	Plate ½ mold*	8/23/12
Middle Room (Clean Room 1)	[redacted]		
5 FLR (near crimp bench)	0	1	2/23/12
6 FLR (near sink bench)	0	3	2/23/12
6 FLR (near sink bench)	2*	11*	3/15/12
MRmisc1 (dh20 gallon)	1	1	5/10/12
Gown Room (Clean Room 2)	[redacted]		
Gown Room Flr	OG*	0	1/26/12
Gown Room Flr	0	1	3/1/12
Gown Room Flr	9*	0	8/9/12
Prep Room (Clean Room 2)	[redacted]		
Prep Room Flr	1	1	2/2/12
Misc #2 PR (top of radio)	0	1	2/7/12
Misc: PR (Calcium chloride bin)	1	1	4/4/12
Prep Room Flr	15*	2*	6/13/12

Note: (*) indicates result over action level; OG indicates over growth

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EMPLOYEE(S) SIGNATURE [redacted]

DATE ISSUED
10/26/12

FORM FDA 483 (09/08) PREVIOUS EDITION OBSOLETE **INSPECTIONAL OBSERVATIONS** Page 3 of 8

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT OFFICE ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
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New England Compounding Pharmacy Inc., d/b/a New England Compounding Center	697 Waverly Street
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DURING AN INSPECTION OF YOUR FIRM WE OBSERVED:

Table #3: Surface Samples of ISO 8 (Class 100,000) Rooms
Alert: 8 CFU Action: 10+ CFU

Location	Result Bacteria	Result Mold	Date
Prep Room (Clean Room 1)	[redacted]		
Misc. Prep room samples (shopping cart handle)	0	OG with mold*	1/6/12
Misc. Prep room samples (metal cart)	1	1	1/26/12
PR (carriage w/blue handle w/scratch marks)	3	1	2/2/12
PR (carriage w/blue handle w/x)	4	1	2/2/12
PR (outside of barrel)	16*	2*	3/1/12
9 FLR (PR) (near entrance)	1	7	3/8/12
PR (blue tamper evident caps, bin)	4	3	3/15/12
PRmisc2 (inside plastic cover to clear plastic bags)	OG*	0	4/5/12
9 FLR prep room (near entrance)	½ plate OG*	0	4/5/12
10 FLR (PR) (under 2nd rack)	3	1	4/12/12
PR MISC 2 (top of lid of white container under rack)	1	1	5/24/12
10 FLR (PR) (back of room area)	OG*	0	5/24/12
10 FLR (PR) (back of room area)	0	3	5/31/12
9 FLR (PR) (entrance area)	OG*	0	6/15/12
10 FLR (PR) (back of room area)	20*	0	6/15/12
10 FLR (PR) (back of room area)	12*	0	6/28/12
9 FLR (PR) entrance area	4*	15*	6/28/12

Note: (*) indicates result over action level; OG indicates over growth

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Table #4: Air Sampling of ISO 6 (Class 1,000) Rooms

Location	Result Bacteria	Result Mold	Date
Middle Room (Clean Room 2)	[redacted]		
Middle room	0	1 big mold	5/29/12

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EMPLOYEE(S) SIGNATURE [redacted]

DATE ISSUED 10/26/12

FORM FDA [redacted] PREVIOUS EDITION OBSOLETE INSPECTIONAL OBSERVATIONS Page 4 of 8

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT OFFICE ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
New England District Office 1 Montvale Ave, Stoneham, MA 02180	10/1-2, 10/4-5, 10/9, 10/15, and 10/26/12
[redacted] Industry Information: www.fda.gov/oc/industry	FEI NUMBER 3003623877

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

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New England Compounding Pharmacy Inc., d/b/a New England Compounding Center	697 Waverly Street
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Framingham, MA 01702	Compounding Pharmacy

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DURING AN INSPECTION OF YOUR FIRM WE OBSERVED:

Table #5: Air Sampling of ISO 7 (Class 10,000) Rooms
Alert: 5 CFU Action: 8+ CFU

Location	Result Bacteria	Result Mold	Date
Gown Room (Clean Room 1)	[redacted]		
Gown room	29*	1*	5/31/12
Gown room	11*	1*	6/28/12
Middle Room (Clean Room 1)	[redacted]		
Crimp Station	3	1	2/23/12
Prep Room (Clean Room 2)	[redacted]		
Prep room	0	1	5/2/12
Gown Room (Clean Room 2)	[redacted]		
Gown room	7*	3*	8/9/12

Note: (*) indicates result over action level

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Table #6: Surface and Air Sampling of ISO 5 (Class 100) Clean Room 2
No Action/Alert Levels specified by firm for ISO 5 (Class 100) areas.

Location	Sample Type	Result Bacteria	Result Mold	Date
Table 1 (near Horiz L & R hoods)	Surface	0	3	1/26/12
Table 1 (near Horiz L & R hoods)	Surface	1	1	5/2/12
Between Horiz L & Horiz R	Air	1	1	7/25/12

There was no investigation conducted by the firm when levels exceeded their action limits and there was no identification of the isolates. No documented corrective actions were taken to remove the microbial contamination (bacteria and mold) from the facility.

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE [redacted]	DATE ISSUED 10/26/12

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

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DURING AN INSPECTION OF YOUR FIRM WE OBSERVED:

4. The environmental monitoring procedure requires sampling via personnel touch plates taken upon completion of sterile compounding and prior to cleaning. Records from January thru September 2012 for Clean Room 1 and Clean Room 2 showed the following results inside production hoods:

Table #1: Clean Room 1 and Clean Room 2 Facility Personnel Touch Plates

Date	Isolates	Location	Product
1/3/12	OG with bacteria	Horizontal 1 (Clean Room 1)	Avastin
4/12/12	OG with bacteria	IT/Hood 3 (Clean Room 1)	Product not documented
6/15/12	1 bacteria, 1 mold	Horizontal 2A (Clean Room 1)	Ropiv/Ketor/Epi
6/21/12	2 bacteria	Horizontal R (Clean Room 2)	Product not documented
7/2/12	½ plate OG with bacteria	Horizontal L (Clean Room 2)	Product not documented
7/19/12	1 bacteria, 2 molds	Horizontal 2C (Clean Room 1)	Mafenide Acetate
7/31/12	2 bacteria	Horizontal 2A (Clean Room 1)	KCl/Lido/D5W
8/16/12	2 bacteria	Hood 3 (glovebox) (Clean Room 1)	Ace 20%, Ped Atropine

Note: OG indicates over growth

These results were not investigated and there was no identification of the isolates. There were no product impact assessments performed for any sterile products that were made in the hoods or gloveboxes on the days the samples were taken. In addition, the firm has no evidence that any corrective actions were taken to prevent contamination of the sterile drug products.

5. The conditions listed below were identified during the inspection in areas used for the preparation, filling, and/or storage of sterile drugs products.

- On 10/04/2012, we observed condensation and what appeared to be tarnished discoloration on the interior surfaces (e.g. chamber) of the "[redacted] autoclave", located in the firm's Middle Room (ISO 7). This autoclave is used for the steam sterilization of formulated bulk drug suspensions, including preservative free formulations of methylprednisolone and triamcinolone, which are intended for injection. Of note, this is the final sterilization step in the process for these products.

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (Print or Type)	DATE ISSUED
	[redacted]		10/26/12

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

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DURING AN INSPECTION OF YOUR FIRM WE OBSERVED:

- On 10/04/2012, we observed greenish yellow discoloration lining the interior surface of the viewing lens within the "Inside" autoclave, located in the firm's Middle Room (ISO 7). This is one of two tabletop autoclaves used for steam sterilization of various components and equipment (e.g. vials of multiple sizes, stoppers, and spin bars) used in the formulation of sterile drug products

- On 10/04/2012, we observed what appeared to be tarnished discoloration on the interior surfaces (e.g. chamber and trays) of the "Outside" autoclave located in the firm's Middle Room (ISO 7). Moreover, condensation was observed along the interior surfaces of the "Outside" autoclave to collect in a pool at the base of the chamber. This is one of two tabletop autoclaves used for steam sterilization of various components and equipment (e.g. vials of multiple sizes, stoppers, and spin bars) used in the formulation of sterile drug products.

- The firm is abutted to the rear and along the left parking area by a recycling facility that handles such materials as mattresses and plastics. On 10/02/2012, the area was observed to include large equipment (e.g. excavators and freight trucks) producing airborne particulates (e.g. dust). Rooftop units serving the firm's HVAC system were estimated to be located approximately 100 feet from the recycling facility.

- On 10/04/2012, we observed what appeared to be dark particulate and white, filamentous substances covering the louvers of an HVAC return located behind the "[redacted] autoclave", located in the firm's Middle Room (ISO 7). This autoclave is used for the steam sterilization of formulated bulk drug suspensions, including preservative free formulations of methylprednisolone and triamcinolone, which are intended for injection.

- On 10/02/2012 and 10/04/2012, we observed yellow residue lining the rear return of Weigh Station 2 Hood and greenish residue lining the rear return of Weigh Station 3 Hood, both located in the firm's ISO 6 Clean Room. The firm uses Weigh Station Hoods to weigh active ingredients and other raw materials utilized in the formulation of sterile drug preparations.

- On 10/04/2012, we observed greenish residue covering the surface of the [redacted] ceiling, exposed to the [redacted] filter above, within Weigh Station 3 Hood located in the firm's ISO 6 Clean Room. The firm uses Weigh Station Hoods to weigh active ingredients and other raw materials utilized in the formulation of sterile drug preparations.

- On 10/04/2012, we observed what appeared to be tarnished discoloration on the interior surfaces (e.g. chamber and trays) of the [redacted] located in the firm's Prep Room (ISO 8). This [redacted] is used to sterilize equipment (e.g. beakers, spatulas, and spoons) used in the formulation of sterile drug products.

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE [redacted]	DATE ISSUED 10/26/12

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CITY, STATE AND ZIP CODE	TYPE OF ESTABLISHMENT INSPECTED
Framingham, MA 01702	Compounding Pharmacy

THIS DOCUMENT LISTS OBSERVATIONS MADE BY THE FDA REPRESENTATIVE(S) DURING THE INSPECTION OF YOUR FACILITY. THEY ARE INSPECTIONAL OBSERVATIONS, AND DO NOT REPRESENT A FINAL AGENCY DETERMINATION REGARDING YOUR COMPLIANCE. IF YOU HAVE AN OBJECTION REGARDING AN OBSERVATION, OR HAVE IMPLEMENTED, OR PLAN TO IMPLEMENT, CORRECTIVE ACTION IN RESPONSE TO AN OBSERVATION, YOU MAY DISCUSS THE OBJECTION OR ACTION WITH THE FDA REPRESENTATIVE(S) DURING THE INSPECTION OR SUBMIT THIS INFORMATION TO FDA AT THE ADDRESS ABOVE. IF YOU HAVE ANY QUESTIONS, PLEASE CONTACT FDA AT THE PHONE NUMBER AND ADDRESS ABOVE.

DURING AN INSPECTION OF YOUR FIRM WE OBSERVED:

- On 10/04/2012, a boiler installed within approximately 30 feet of the entrance to the Prep Room (ISO 8) was observed to be leaking water into puddles. Moreover, wet floor surfaces around the boiler appeared to be soiled with thick white debris and thick black, granular material. Gaps were observed between sliding doors, located at the transition between the Prep Room (ISO 8) and the warehouse, despite being fully closed. This room is used for the preparation of equipment and includes the [redacted]

- On 10/02/2012, the tacky mat located within the entrance of the Prep Room (ISO 8), at the transition to the warehouse, was observed to be brown and soiled. This room is used for the preparation of equipment and includes the [redacted]

- On 10/04/2012, we observed cloudy discoloration on the [redacted] barrier [redacted], facing the ISO 6 Clean Room, and metal surfaces within the "Pass Thru," installed within the wall of the ISO 6 Clean Room. Moreover, the metal ledge, within the ISO 6 Clean Room, was observed to contain reddish-brown and cloudy substances. The firm utilizes the ISO 6 Clean Room to formulate and fill sterile preparations, including methylprednisolone.

- On 10/04/2012, we observed what appeared to be dark, hair-like discoloration along the gasket and crevices located at the bottom edge of the closed pass through installed within the wall of the ISO 6 Clean Room. The firm utilizes the ISO 6 Clean Room to formulate and fill sterile preparations, including methylprednisolone.

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE [redacted]	DATE ISSUED 10/26/12

Barry Cadden and New England Compounding Center-
Advisory Letter: dated—9/30/2004 to Barry Cadden,
RE Dkt. Nos. DS-03-060 & PH-03-070

The Commonwealth of Massachusetts
Executive Office of Health and Human Services
Department of Public Health
250 Washington Street, Boston, MA 02108-4619

Board of Registration in Pharmacy
239 Causeway Street, 5th Floor
Boston, MA 02114

MITT ROMNEY
GOVERNOR

KERRY HEALEY
LIEUTENANT GOVERNOR

RONALD PRESTON
SECRETARY

CHRISTINE C. FERGUSON
COMMISSIONER

September 30, 2004

Barry Cadden, R.Ph.
Manager of Record
New England Compounding Center
697 Waverly Street
Framingham, MA 01702

Re: In the Matter of:
In the matter of DS-03-060 and PH-03-070 – New England Compounding Center (Permit # 2848).

Dear Mr.. Cadden:

The Board has voted to resolve the above-referenced cases by means of issuing an Advisory Letter to you and New England Compounding Center. Enclosed for your record is a copy of the final decision letter is the above referenced matter.

Please contact me at (617) 727-6095 if you have any questions regarding this matter.

Sincerely,

Charles R. Young, R.Ph.
Executive Director
Massachusetts Board of Registration in Pharmacy
239 Causeway Street, Suite 5
Boston, MA 02114

Enclosure: Advisory Dismissal Letter
Dated: September 30, 2004
Board Decision ID Number:

The Commonwealth of Massachusetts
Executive Office of Health and Human Services
Department of Public Health

Board of Registration in Pharmacy
239 Causeway Street, 5th Floor
Boston, MA 02114
(617) 727-9953

In the Matter of:	)	
New England Compounding	)	
Center	)	
697 Waverly Street	)	
Framingham, MA 01702	)	Docket No. DS-03-060
Registration No. 2848	)	PH-03-070
& Barry Cadden, R.Ph.	)	
License No.21239	)	
	)	

ADVISORY LETTER

The Board of Registration in Pharmacy ("Board") received a complaint from a concerned Texas pharmacist about products being solicited by Barry Cadden, R.Ph., License No. 21239 ("Registrant") and New England Compounding Center, License No. 2848 (the Pharmacy). The investigation revealed that the solicitations were offering intravitreal triamcinolone acetonide and included promotional material and terminology in the advertisements.

The Board has carefully reviewed the investigative reports and other information provided by the parties regarding the Complaint. The Board determined on September 21, 2004, the Complaint should be resolved by the issuance of this **Advisory Letter** regarding the advertising and solicitation of this product. Although an Advisory Letter does **not** constitute disciplinary action, this letter does communicate the Board's concern regarding the conduct that was the basis for the Complaint. The Board expects a dedicated company response to insure that the factors contributing to the complaints are identified and that appropriate quality assurance measures are implemented to reduce the risk of recurrence of this type of incident.

Please be advised that any failure of the Pharmacy to comply with any of the terms or conditions of this Advisory Letter may be a basis for the Board to reconsider this matter and reopen the Complaint.

BOARD OF REGISTRATION IN PHARMACY

James T. Devita, R.Ph., President

Date: September 30, 2004

cc: Complainant

Board Dec. No.

***Barry Cadden and New England Compounding Center* –**
Advisory Letter: dated—9/30/2004,
RE Dkt. Nos. DS-04-062 & SA-04-161

The Commonwealth of Massachusetts
Executive Office of Health and Human Services
Department of Public Health

Board of Registration in Pharmacy
239 Causeway Street, 5th Floor
Boston, MA 02114
(617) 727-9953

MITT ROMNEY
GOVERNOR

KERRY HEALEY
LIEUTENANT GOVERNOR

RONALD PRESTON
SECRETARY

HRISTINE C. FERGUSON
COMMISSIONER

In the Matter of: New England Compounding Center 697 Waverly Street Framingham, MA 01072 Registration No. 2848 & Barry Cadden, R.Ph. License No.21239	Docket No. DS-04-062 SA-04-161

ADVISORY LETTER

The Board of Registration in Pharmacy ("Board") received complaints from an Iowa pharmacist and Wisconsin Pharmacist alleging that Barry Cadden, R.Ph., License No. 21239 ("Registrant") and New England Compounding Center, License No. 2848 (the Pharmacy) were soliciting out of state prescriptions for office use and using a form unapproved by the Department of Public Health and Board.

The Board has carefully reviewed the investigative reports and other information provided by the parties regarding the Complaint. The Board determined on September 21, 2004, the Complaint should be resolved by the issuance of this **Advisory Letter** regarding the filling of the prescription in this matter. Although an Advisory Letter does not constitute disciplinary action, this letter does communicate the Board's concern regarding the conduct that was the basis for the Complaint. The Board expects a dedicated company response and employee counseling where appropriate to insure that the factors contributing to the complaints are identified and that appropriate quality assurance measures are implemented to reduce the risk of recurrence of this type of incident.

The Board also determined that to close this matter without formal disciplinary action, the Pharmacy must within thirty days of the date of this letter cease using the

"purported prescription form", as it is not compliant with 105CMR § 721.030 et seq and G.L. c. 112 § 12D..

Please be advised that any failure of the Pharmacy to comply with any of the terms or conditions of this Advisory Letter may be a basis for the Board to reconsider this matter and reopen the Complaint.

BOARD OF REGISTRATION IN PHARMACY

James T. Devita, R.Ph., President

Date: September 30, 2004

cc: Complainant

Board Dec. No.

Barry Cadden and New England Compounding Center-
Advisory Letter: dated—9/30/2004 –
RE Dkt. Nos. DS-03-036 & PH-03-042

The Commonwealth of Massachusetts
Executive Office of Health and Human Services
Department of Public Health
250 Washington Street, Boston, MA 02108-4619

Board of Registration in Pharmacy
239 Causeway Street, 5th Floor
Boston, MA 02114

MITT ROMNEY
GOVERNOR

KERRY HEALEY
LIEUTENANT GOVERNOR

RONALD PRESTON
SECRETARY

CHRISTINE C. FERGUSON
COMMISSIONER

September 30, 2004

Barry Cadden, R.Ph.
Manager of Record
New England Compounding Center
697 Waverly Street
Framingham, MA 01702

Re: In the Matter of:
In the matter of DS-03-036 and PH-03-042 – New England Compounding Center (Permit # 2848).

Dear Mr. Cadden:

The Board has voted to resolve the above-referenced cases by means of issuing an Advisory Letter to you and New England Compounding Center. Enclosed for your record is a copy of the final decision letter is the above referenced matter.

Please contact me at (617) 727-6095 if you have any questions regarding this matter.

Sincerely,

Charles R. Young, R.Ph.
Executive Director
Massachusetts Board of Registration in Pharmacy
239 Causeway Street, Suite 5
Boston, MA 02114

Enclosure: Advisory Dismissal Letter
Dated: September 30, 2004
Board Decision ID Number:

The Commonwealth of Massachusetts
Executive Office of Health and Human Services
Department of Public Health

MITT ROMNEY
GOVERNOR

KERRY HEALEY
LIEUTENANT GOVERNOR

RONALD PRESTON
SECRETARY

CHRISTINE C. FERGUSON
COMMISSIONER

Board of Registration in Pharmacy
239 Causeway Street, 5th Floor
Boston, MA 02114
(617) 727-9953

In the Matter of: New England Compounding Center 697 Waverly Street Framingham, MA 01702 Registration No. 2848. & Barry Cadden, R.Ph. License No.21239	Docket No. DS-03-036 PH-03-042

ADVISORY LETTER

The Board of Registration in Pharmacy ("Board") received reports from a surgical center in Rapid City, SD expressing concern about products being solicited by Barry Cadden, R.Ph., License No. 21239 ("Registrant") and New England Compounding Center, License No. 2848 (the Pharmacy). The investigation revealed that the solicitations were out of state prescriptions for office use and using a form unapproved by the Department of Public Health and Board.

The Board has carefully reviewed the investigative reports and other information provided by the parties regarding the Complaint. The Board determined on September 21, 2004, the Complaint should be resolved by the issuance of this **Advisory Letter** regarding the filling of the prescription in this matter. Although an Advisory Letter does **not** constitute disciplinary action, this letter does communicate the Board's concern regarding the conduct that was the basis for the Complaint. The Board expects a dedicated company response and employee counseling where appropriate to insure that the factors contributing to the complaints are identified and that appropriate quality assurance measures are implemented to reduce the risk of recurrence of this type of incident.

The Board also determined that to close this matter without formal disciplinary action, the Pharmacy must within thirty days of the date of this letter cease using the

"purported prescription form", as it is not compliant with 105CMR § 721.030 et seq and G.L. c. 112 § 12D.

Please be advised that any failure of the Pharmacy to comply with any of the terms or conditions of this Advisory Letter may be a basis for the Board to reconsider this matter and reopen the Complaint.

BOARD OF REGISTRATION IN PHARMACY

James T. Devita, R.Ph., President

Date: September 30, 2004

cc: Complainant

Board Dec. No.

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT OFFICE ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
One Montvale Avenue Stoneham, MA 02180 [redacted]	04 / 9, 10, and 16 / 2002
	FEI NUMBER 3003623877

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: Barry Cadden, R. Ph, Owner and Director of Pharmacy

FIRM NAME	STREET ADDRESS
New England Compounding Pharmacy, Inc.	697 Waverly Street
CITY, STATE AND ZIP CODE	TYPE OF ESTABLISHMENT INSPECTED
Framingham, MA 01702	Compounding Pharmacy

DURING AN INSPECTION OF YOUR FIRM (I) (WE) OBSERVED:

1. Betamethasone Repository Injection (Betamethasone Acetate and Betamethasone Sodium Phosphate Suspension 6 mg/ml), a product which is intended to be sterile, is sampled for sterility and endotoxin testing immediately after sterilization of the bulk compounded product in a 1000-ml beaker. Individual vials of Betamethasone Repository are not filled until the test results for sterility and endotoxin (pyrogen) are received from the contract testing laboratory, a process which can take up to one week after the sterilization and sampling of the bulk product have occurred. While laboratory test results are pending, the 1000-ml beaker and its contents are stored in the firm's laminar flow hood. The only other measure taken during this period to prevent recontamination of the bulk suspension is the use of a covering of multiple layers of aluminum foil over the mouth of the beaker.

2. The samples taken immediately after completion of the autoclave sterilization cycle (134° for 20 minutes) are not representative of product that remains in the original 1000-ml beaker for up to one week past the time of sampling.

3. The firm's validation of the autoclave cycle does not take into account the fact that the autoclaved bulk product is not transfilled into a final container/closure system (vials) for a period of up to one week.

4. On at least one occasion, a lot number (Lot 02 01 2002@027) was generated in the firm's computerized record keeping system, for which no associated records could be retrieved. It cannot be determined whether:

- this lot was distributed and records covering its preparation were never created or are no longer in existence, or
- the preparation of this lot never proceeded, but no record of its cancellation was entered in the record keeping system

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (Print or Type)	DATE ISSUED
		[redacted] Investigator [redacted], Investigator [redacted], Compliance Officer	04 / 16 / 2002

NEW ENGLAND COMPOUNDING PHARMACY INC.
697 WAVERLY STREET
FRAMINGHAM, MA 01702
EI 4/9, 4/10, 4/16/02 **CDS/KJ/ML** **PAGE 1**

REASON FOR INSPECTION

This investigation was initiated from HFD-330, Division of Prescription Drug Compliance and Surveillance. HFD-330 requests follow-up of 2 MedWatch Adverse Event Reports. The assignment was entered into FACTS under ID #298826 as a domestic investigation to be conducted under PAC 56D015. The assignment also requests working jointly with the Mass Board of Pharmacy.

HISTORY

There is no pervious investigational/inspectional history on file for New England Compounding (NEC) Pharmacy Inc., Framingham, MA 01702. The Mass Pharmacy Board has inspected NEC in the past.

SUMMARY OF FINDINGS

This investigation of New England Compounding Pharmacy Inc., Framingham, MA 01702 revealed that the subject lot, 02012002@27 identified in MedWatch Forms, could not be traced through NEC Pharmacy records. The owner of NEC, Barry Cadden, R.Ph could offer no definitive explanation/or records. According to Mr. Cadden lot #02012002@27 did not exist. A review of the compounding operations was accomplished and areas of concern regarding sterility were discussed. An FD-483 was issued regarding sterility issues and lack of lot accountability.

The Mass Board of Pharmacy performed their own independent inspection while the FDA investigation was in progress.
Note: Mass Board of Pharmacy was invited to participate by the FDA NWE-DO, per Headquarters' assignment.

PERSONS INTERVIEWED/AREAS OF RESPONSIBILITY

On 4/9/02 credentials were displayed and a Notice of Inspection was issued to Barry J. Cadden R.Ph, Owner & Director of the Pharmacy.

Mr. Cadden coordinated all the information for this report. Mr. Cadden is the Owner of NEC. He identified his wife Lisa Cadden R.Ph as Vice President of NEC. Mrs. Cadden was introduced on the second day of the inspection.

Mr. Cadden was informed that the purpose for the inspection was a follow-up to adverse events involving the compounded product Betamethasone acetate/betamethasone sodium phosphate. (The drug was administered via an epidural injection in the adverse event reports.) Note: Per instruction from HFD-330, detailed information such as lot number & MedWatch Reporter was not shared with Mr. Cadden for confidentiality reasons.)

Mr. Cadden stated there are 8 employees, three of whom are involved in compounding. Mr. Cadden is the only individual that compounds sterile product. NEC has been in business about 4 years.

On the first day of inspection. Mr. Cadden was cooperative & supplied some documents. The second day of inspection, Mr. Cadden had a complete change in attitude & basically would not provide any additional information either by responding to questions or providing records. Mr. Cadden challenged FDA jurisdiction/authority to be at his pharmacy. He indicated he had consulted with his lawyer. From that point on it was essentially "talk to my lawyer".

JURSDICTION

Section 704(a)(2)(A) of the Federal Food, Drug, and Cosmetic Act describes the nature of FDA inspectional authority with regard to retail pharmacies. In particular, this section states that the "provisions of the second sentence of paragraph (1) shall not apply" to pharmacies operating in the retail capacity. The sentence being referred to is contained in Section 704(a)(1)(B). It provides the authority during factory inspections of firms that manufacture, process, pack, or hold prescription and nonprescription human drugs an (restricted) devices for access to "records, files, papers, processes, controls, and facilities" bearing on whether these products are in violation of the Act. In summary, our inspectional authority at pharmacies operating in a retail capacity consists of being able to:

- enter, at reasonable times (Section 704(a)(1)(A), and
- inspect, at reasonable times, and within reasonable limits and in a reasonable manner (Section 704(a)(1)(b), the establishment and its equipment and operations

However, the owner of the pharmacy is not obligated to furnish records, as is normally the case when a facility that processes drug products is being inspected.

NEW ENGLAND COMPOUNDING PHARMACY INC.
697 WAVERLY STREET
FRAMINGHAM, MA 01702
EI 4/9, 4/10, 4/16/02 **CDS/KJ/ML** **PAGE 3**

On the first day of the inspection (April 9) we were allowed to review and were furnished with copies of records related to the compounding of Betamethasone Repository Injection. Later the same day, Mr. Cadden raised as an issue the precise nature of FDA's authority to inspect retail pharmacies. However, at this time he did not express any reservations about having allowed us to review any of these records.

However, it became clear, upon our return on the following morning, that Mr. Cadden had reconsidered this matter. He presented us with a printed copy of Title 21 of the United States Code, Section 374 (the codified version of Section 704 of the Act) that he had apparently downloaded from the Internet (www4.law.cornell.edu/uscode/21/374.html), with paragraph (2)(A) of Section 374 highlighted. Mr. Cadden stated that he was no longer willing to provide us with any additional records, unless we would identify the specific lot of Betamethasone Repository Injection that was the focus of this investigation. Since we had been specifically directed by CSO [redacted] (CDER/OC/Division of Prescription Drug Compliance and Surveillance) not to divulge this lot number, we were not in a position to comply with Mr. Cadden's request. From this point on, no additional records were provided or collected.

MEDWATCH ADVERSE EVENTS

Per HFD-330 Assignment, 2 Adverse Events, reported through the MedWatch system were identified to the NWE-DO for follow-up. The information contained in these reports were not openly shared with NEC nor with Mass Board of Pharmacy. Both MedWatch reports were from the same Reporter and involved the same lot number of Betamethasone.

Note: An Inspection/subsequent action of a California Compounding Pharmacy for Betamethasone was revealed during a telecon with HFD-330 while the NEC investigation was in progress. (The information was not included with the NWE-DO assignment.) Very similar operational problems existed with the California Compounding Pharmacy that were encountered with NEC. The action for the California Compounding Pharmacy was taken by the State Pharmacy Board. See Attachments to this report for the FD-483 and State Board of Pharmacy, California Case #2427 Accusation.

The NWE-DO FDA Investigators conducted the NEC MedWatch follow-up investigation by requesting a printout of the Betamethasone Compounded Product for the year 2002. The subject lot number was listed on this printout, i.e., lot #02012002@27. See Exhibit #1 for this printout.

NEW ENGLAND COMPOUNDING PHARMACY INC.
697 WAVERLY STREET
FRAMINGHAM, MA 01702
EI 4/9, 4/10, 4/16/02 **CDS/KJ/ML** **PAGE 4**

From this printout, lot #'s 02152002@10 and 02012002@27 were selected for review. Formula Worksheets for lot #02152002@10 were provided, see Exhibit #2. No records for lot #02012002@27, (the MedWatch lot number), were provided. Mr. Cadden indicated that there were no Compounding records for this lot. When he accessed the database, the only document generated was a Prescription log with a "date made", of 2/1/02 for 1000 ml. See Exhibit #3.

Mr. Cadden expressed his belief that the Betamethasone was never compounded under lot #02012002@27. However he could not provide any documents to support his belief, such as a cancelled lot etc.

Due to MedWatch confidentiality restrictions, the status of the subject lot could not be pursued via this avenue.

Note: Complaint files are not maintained per se. Mr. Cadden stated that complaints are kept within a Customer file. FDA could not reveal the Complainant to Mr. Cadden.

The FDA Investigators then contacted the MedWatch Reporter in an attempt to verify the existence of lot #02012002@27. The Reporter, (b)(6), (b)(7)(C) was contacted by phone. The contact person was identified to FDA as (b)(6), (b)(7)(C).

(b)(6), (b)(7)(C) stated that a total of probably 5 incidents occurred after using subject Betamethasone on patients. The two more recent incidents were reported via MedWatch. Refer to MedWatch Reports for details. They are Assignment Attachments to this report.

(b)(6), (b)(7)(C) said he had no product remaining, all had been returned to NEC. He stated that he spoke to 'Barry' by phone describing the incidents but did not tell him he was reporting adverse events on MedWatch Forms.

(b)(6), (b)(7)(C) reviewed his paperwork, including PO Invoice, Return Goods, but could not find any paperwork specifically identifying the subject lot.

(b)(6), (b)(7)(C) stated he would provide copies of these documents to the FDA NWE-DO. They were faxed the same day and hard copies would be mailed overnight. See Attachments for these records. Note: There is no lot number identified on any of the records provided by (b)(6), (b)(7)(C)

was asked specifically if FDA could share the MedWatch Reports with Mr. Cadden. (b)(6), (b)(7)(C) said he would not want the information shared.

NEW ENGLAND COMPOUNDING PHARMACY INC.
697 WAVERLY STREET
FRAMINGHAM, MA 01702
EI 4/9, 4/10, 4/16/02 **CDS/KJ/ML** **PAGE 5**

Note: A follow-up assignment at the [redacted] location should be considered if HFD-330 deems it appropriate.

Due to jurisdiction/confidentiality restrictions, this FDA investigation could not proceed to any definitive resolution of issues raised in the Headquarter's assignment. HFD-330 Assignment contacts, [redacted] and Kathy Anderson were fully informed of problems/barriers that were encountered throughout the inspection. NWE-DO Compliance Director, David Elder and NWE-DO Drug SI, [redacted] were also made aware of the situation.

Prior to concluding the investigation, poor practices and areas of concern were discussed via Conference Call with HFD-330 and NWE-DO Management. The FDA Investigators were encouraged to issue an FD-483 to NEC.

The FDA Investigators impressed upon HFD-330 and NWE-DO Management that due to limitations on information gathering and access to records, the FD-483 observations could not/would not be supported with documentation. The FDA Investigators were directed to issue the 483 (even in light of the lack of documentation).

The FD-483 was faxed to HFD-330 for review and comment prior to issuance. [redacted] and Kathy Anderson deleted 3 of the 7 Observations and modified one observation, (#5) by removing the lot number identification.

A conference call involving NWE-DO Investigators, HFD-330 [redacted] Kathy Anderson and CDER FOI Specialists [redacted] was held on 4/15/02. FOI Specialists had no problem including the lot number on the observation. This was based on the fact that the suspect lot number was never revealed to NEC as the suspect lot number on the MedWatch Form.

The modified 483 was issued on 4/16/02 with 4 observations listed. Numbers 1-3 involved sterility issues. Observation 4 essentially described lack of lot number accountability. Refer to List of Observations for details, an attachment to this report.

OPERATIONS

The firm is a compounding pharmacy. The hours of operation are Monday through Friday 9 am to 5 pm. All information was obtained from Mr. and Mrs. Cadden. There are 8 employees total, including 2 Registered Pharmacists, 1 data entry, 2 secretarial staff, and 3 pharmacy technicians. Pharmacists and Technicians receive Compounding Technique Certification (30 hours) from Professional Compounding Centers of America (PCCA, Houston, Texas).

NEW ENGLAND COMPOUNDING PHARMACY INC.
697 WAVERLY STREET
FRAMINGHAM, MA 01702
EI 4/9, 4/10, 4/16/02 **CDS/KJ/ML** **PAGE 6**

Formulations for compounding are obtained from PCCA. The firm's prescription software (PK Software) is from PCCA. Raw materials are obtained primarily from PCCA, with alternate source Spectrum (New Brunswick, NJ). Certificates of Analysis are provided with Spectrum products. COA's were provided with PCCA products on request. See Exhibit #'s 4(a-b) for representative examples. Sterile compound product samples are sent to Analytical Research Labs (Oklahoma City, OK) for sterility and endotoxin testing.

Medications are compounded pursuant to written/telephone/fax prescriptions from physicians/licensed facilities. The firm deals directly with patients, physicians and institutions. The firm states they fill patient specific prescriptions only, and that they have no wholesale functions. See Exhibit #5 for a representative Order Form. Mr. Cadden states that he is the only employee who compounds sterile products.

[redacted] R.Ph, from the Massachusetts Board of Pharmacy conducted her own independent audit on the second FDA on-site inspection of 4/10. [redacted] was made aware of our concerns/findings regarding the Betamethasone Repository 6mg/ml injectable. Investigator [redacted] accompanied [redacted] for a State general inspection. Additional findings included:

1) Absence of DEA license on premises
2) Absence of DEA Class II Narcotic inventory on premises
3) Medication refrigerator contained employee beverages
4) Medications (ketoprofen, specifically) are commonly transferred from large bulk container to smaller (ketoprofen) container for ease of dispensing (therefore medication would be transferred to smaller container with incorrect lot and expiration date).
5) No reverse distributor for disposal of unused/unacceptable materials

The firm compounds betamethasone product both with (multi-dose vial) and without (single dose vial) preservative. Limited information about the compounding process was obtained. Mr. Cadden states he uses a Log Formulation Worksheet (LFW) (Exhibit #2) which outlines the steps taken in compounding the betamethasone. We were denied a copy of the PCCA formulation used to derive the Log Formulation Worksheet (LFW). A copy of the firm's "Policies & Procedures for Compounding Sterile Products" was obtained (Exhibit #6). The medication name on this document is "hyaluronidase", but Mr. Cadden claims this document applies to all sterile products. It outlines controls for the facility, equipment, maintenance, personnel, quality assurance/control, and dispensing. The lot in question from the MedWatch reports was lot #02012002@27, which contained preservative according to firm records. See Exhibit #1 for lot number printout.

NEW ENGLAND COMPOUNDING PHARMACY INC.
697 WAVERLY STREET
FRAMINGHAM, MA 01702
EI 4/9, 4/10, 4/16/02 **CDS/KJ/ML** **PAGE 7**

Mr. Cadden states when compounding the product, he accesses the LFW in the computer. The computer assigns a lot number based on the date and order of compounding (i.e.: 02012002@27 would've been the 27th item entered in the computer for compounding on February 1, 2002). He then determines the quantity to compound and prints the LFW. The product is made according to the quantities and directions on the LFW. The location where raw materials are mixed is unclear. Mr. Cadden stated that he then covered the mixture in the beaker with aluminum foil and placed it in the autoclave for 20 minutes at 134° (the autoclave is located outside of the clean room). Then he brings the compound to room temperature in the beaker on the magnetic stirrer (2-4 hours) due to the suspending agent. He then takes suspension from the beaker and transfers it to vials. The vials are labeled with self made computer labels. See Exhibit #7 for a representative example of a label. A sample is sent to ARL for sterility and endotoxin testing. Mr. Cadden states he waits for acceptable lab results before dispensing product.

Mr. Cadden stated on/about 3/19/02 through 4/6/02 he received ARL results positive for endotoxin (greater than 100 ppb). See Exhibit #'s 8(a-d) for Test Results. He stated these lots (about 4 lots total) were awaiting disposal at his facility. After research, Mr. Cadden decided to change the suspending agent carboxy methylcellulose to polygiycol. After making a lot on 4/6/02, Mr. Cadden stated he sent his samples to ARL, then left the product beaker covered with aluminum foil on the magnetic stirrer in the hood awaiting lab results. Mr. Cadden told us it could take anywhere from seven to ten days to obtain lab results. This beaker was observed in the laminar flow hood on 4/9/02. When questioned about this practice, Mr. Cadden stated he didn't want to waste the money on vials or the effort in transfilling the vials if the 4/6/02 lot failed testing. He stated he would transfill the vials upon receiving satisfactory lab results. It was discussed with Mr. Cadden that this was not an acceptable process for maintaining product sterility. Upon returning to the firm 4/10/02, the hood was clean and Mr. Cadden was asked the whereabouts of the 4/6/02 lot. He stated he received negative lab results the night before and had transfilled the lot into vials that morning. He accredited the positive endotoxins to the previous suspending agent. When asked if he had intentions of dispensing the lot, he said yes. The FDA investigator suggested to Mr. Cadden that he retest the 4/6/02 lot again after transfilling the vials since the product sat in a beaker for 5 days before transfilling into vials. The risks and impacts of non-sterile product to patients and his firm were discussed. Mr. Cadden agreed to retest the lot to confirm sterility and lack of endotoxins.

NEW ENGLAND COMPOUNDING PHARMACY INC.
697 WAVERLY STREET
FRAMINGHAM, MA 01702
EI 4/9, 4/10, 4/16/02 **CDS/KJ/ML** **PAGE 8**

AREAS OF CONCERN

1) No accessible system for retrieving complaints/ADR reports. The firm claims that these documents are filed under patients or institutions, so they cannot be retrieved without that specific information. This prohibits the firm from identifying and tracking problems with individual medications or lot numbers.

2) Beyond use dating not substantiated. Preservative and Preservative Free product both receive the same expiration date of six months. There is no indication as to why/how this date was chosen and if laboratory data confirms these expiration dates.

3) Preservative vs. preservative free: The only label differentiation between the two is"***MDV***" and "PF".

4) Batch formula worksheets contain expired products. Mr. Cadden states they use in date materials, but probably have not updated their computer with correct lot numbers and dates. If raw materials were to be recalled, the firm would have trouble recalling their correct products since it is not apparent what lots are used for compounding medications.

5) Recordkeeping poor; lot numbers exist with no prescriptions linked as being dispensed. This would again prohibit timely recall of product to patients.

6) Positive endotoxin source still definitively unknown.

7) Non-sterile laminar flow hood environment: On the first day of the investigation, the clean room was observed. The laminar flow hood contained a beaker covered with aluminum foil on a magnetic stirrer. To the left of the beaker sat two-three bags of vial caps. To the right of the beaker sat a plastic (Rubbermaid-like) tray with miscellaneous items. When asked about this practice, Mr. Cadden acknowledged that there were unsterile items placed in the hood, but that he tried to wipe them down with alcohol before placing them inside the hood.

8) Autoclave: there is no SOP in place for use of or maintenance of the autoclave. Mrs. Cadden says the machine is "cleaned/flushed" weekly on Friday night. There is no documentation to support this statement, which was also noted by the state representative.

NEW ENGLAND COMPOUNDING PHARMACY INC.
697 WAVERLY STREET
FRAMINGHAM, MA 01702
EI 4/9, 4/10, 4/16/02 **CDS/KJ/ML** **PAGE 9**

ASSIGNMENT QUESTIONS

The following represents information gathered to address specific questions included in the assignment. (Refer to the Assignment for the list of questions.) The information is supplied in the same sequence as the questions are asked in the assignment.

#1 This question is to be answered by the Mass Board of Pharmacy.

#2 yes

#3 •they sometimes have a week's worth of product on hand
•1000 ml compounded
•dispension timeframe varies

#4 no, supposedly they do not sell wholesale

#5 •they do not dispense directly to patients
•yes, they provide to institutional pharmacy for dispensing to patients

#6 •they dispense 200/300 Rx's per month
•about 50% out of state

#7 see EIR

#8 not provided

#9 refer to EIR, some COA's on file

#10 no formal written complaint system
Supposedly complaints are kept within a Customer File.

DISCUSSION WITH MANAGEMENT

At the conclusion of inspection, an FD-483 List of Observations was issued to Barry J. Cadden, R.Ph, Director of Pharmacy & Owner of NEC. Also present was [redacted] Administrative Assistant. [redacted] was present on 4/10/02 and at the closing on 4/16/02. Essentially [redacted] presence was as 'note taker'.

All 3 FDA Investigators were present. The Observations included:

NEW ENGLAND COMPOUNDING PHARMACY INC.
697 WAVERLY STREET
FRAMINGHAM, MA 01702
EI 4/9, 4/10, 4/15/02 **CDS/KJ/ML** **PAGE 10**

Observation #1 **Betamethasone Repository Injection (Betamethasone Acetate and Betamethasone Sodium Phosphate Suspension 6 mg/ml, a product which is intended to be sterile, is sampled for sterility and endotoxin testing immediately after sterilization of the bulk compounded product in 1000-ml beaker. Individual vials of Betamethasone Repository are not filled until the test results for sterility and endotoxin (pyrogen) are received from the contract testing laboratory, a process which can take up to one week after the sterilization and sampling of the bulk product have occurred. While laboratory test results are pending, the 1000-ml beaker and its contents are stored in the firm's laminar flow hood. The only other measure taken during this period to prevent recontamination of the bulk suspension is the use of a covering of multiple layers of aluminum foil over the mouth of the beaker.**

In response to item #1, Mr. Cadden stated it was not his usual practice to wait for up to one week before filling individual vials. He stated the practice of transfilling the vials normally occurs within a few hours after autoclaving, once cooling of the beaker with product mixture is complete. He stated the delay (of up to one week) in transfilling only occurred during the period in which product samples were testing positive for endotoxin, and it was for that reason he did not want to transfill the vials unless the sample received satisfactory laboratory analysis. It was explained to Mr. Cadden that these observations were discussed with him during the investigation, but Mr. Cadden declined to provide documentation showing this was not his normal practice. Mr. Cadden also stated that the beaker with product witnessed by FDA investigators actually didn't contain the betamethasone repository. Mr. Cadden was reminded of the contradictory information he provided to the investigators during the investigation.

Observation #2 **The samples taken immediately after completion of the autoclave sterilization cycle (134° for 20 minutes) are not representative of product that remains in the original 1000-ml beaker for up to one week past the time of sampling.**

In response to item #2, Mr. Cadden stated it was incorrect because item #1 was incorrect per above.

Observation #3 **The firm's validation of the autoclave cycle does not take into account the fact that the autoclaved bulk product is not transfilled into a final container/closure system (vials) for a period of up to one week.**

In response to item #3, Mr. Cadden stated it was incorrect because item #1 was incorrect per above.

Observation #4 **On at least one occasion, a lot number (Lot 02012002@27) was generated in the firm's computerized recordkeeping system, for which no associated records could be retrieved. It cannot be determined whether:**

- **this lot was distributed and records covering its preparation were never created or are no longer in existence, or**
- **the preparation of this lot never proceeded, but no record of its cancellation was entered into the recordkeeping system**

See Exhibit #'s 1 and 3 to support this observation.

In response to item #4, Mr. Cadden stated he agreed with this observation. He also stated that of the two possibilities, he agreed with the latter the most.

Mr. Cadden indicated he would consider a written response to the 483 Observations but was basically non-committal.

The inspection was concluded.

This investigative report was prepared by all 3 FDA Consumer Safety Officers. Primary responsibility for Headings included:

- [redacted] MedWatch Section
- [redacted] Operations Section
- [redacted] Compliance Officer, Jurisdiction Section

NEW ENGLAND COMPOUNDING PHARMACY INC.
697 WAVERLY STREET
FRAMINGHAM, MA 01702
EI 4/9, 4/10, 4/16/02 **CDS/KJ/ML** **PAGE 12**

EXHIBITS

#1 2002 Betamethasone lot number Printout
#2 Representative Formula Worksheet
#3 Prescription Log, 1 page
#4 Certificates of Analysis
(a) Spectrum
(b) PCCA
#5 Representative Order Form
#6 Policies & Procedures, Sterile Products
#7 Representative Vial label
#8 ARL Results
(a) #21119 (c) #21178
(b) #21162 (d) #21179

ATTACHMENTS

FD-482 Notice of Inspection
FD-483 List of Observations
FACTS Assignment ID #298826
HFD-330 Assignment dated 4/4/02
HFD-330 FAX dated 4/9/02, 18 pages
Related MedWatch Information sent to NWE-DO from Reporter

[redacted]
US FDA NWE-DO

[redacted]
US FDA NWE-DO

[redacted]
US FDA NWE-DO

CDS/KJ/ML/lcj:4/19,22,23,24/02 a:/NECPI.EIR

Distribution:

O: EIR, Exhibits, Attachments to New England Compounding Pharmacy
FEI 3003623877
cc: EIR, Exhibits, Attachments to HFD-330, Attn: [redacted]
cc: EIR only, Compliance Branch, Attn: [redacted] NWE-DO

MDPH-Division of Health Professions Licensure
INVESTIGATION REPORT

Licensee Name:	Docket No.
New England Compounding Center And Barry Cadden	DS 03 055 PH 03 066

Priority Code: 2 **Received by DHPL: 2/12/2003** **Docket Opened:** 2/12/03 **Assigned:** 2/12/03

Investigator Name: Leslie S. Doyle, Compliance Officer

Supervisor Name: Jean Pontikas - Director

SECTION I: Demographics and History

A. Licensee Information

1. **Name of Licensee/Respondent:**

   Barry Cadden

2. **Address of Record:**

   [redacted]

3. **Phone Number(s):**

   Home: [redacted] **Cell:** (N/A) **Business:** (508) 820 0606

4. **Licensee/Respondent Date of Birth:** [redacted]

5. **License Type & No.:** PH 21239 **Current Status:** C **Exp. Date:** 12/31/04

6. **Prior Discipline (explain):**

Both pharmacist and pharmacy have prior complaint history - the specifics are stated below.

7. **Original Date of Issuance:**

DS - New England Compounding Center issued 7/16/1998 DS 2848
PH - Barry Cadden - Manager of record issued 10/9/1990 PH 21239

8. **Record of Standing attached:** **X Yes** ☐ No

   If not, complete item 9 below:

9. **Name of Educational Institution Attended:**

   University of Rhode Island
   Date of Graduation: 1990

MDPH-Division of Health Professions Licensure
INVESTIGATION REPORT

Licensee Name:	Docket No.
New England Compounding Center And Barry Cadden	DS 03 055 PH 03 066

B. OTHER MASSACHUSETTS LICENSES HELD:

1. Profession/Trade: NA
2. License No. Current Status: Exp. Date:
3. Prior Discipline (explain):
4. Certified Documentation Attached ☐ Yes X No

C. NON-MASSACHUSETTS LICENSES HELD:

1. Profession / Trade: Pharmacy licenses are held in all but four states throughout the United States.
2. License No. Current Status: Exp. Date:
3. Prior Discipline (explain):
4. Certified Documentation Attached ☐ Yes X No

D. LICENSEE'S EMPLOYMENT INFORMATION:

1. Current Employer: New England Compounding Center
2. Address: 697 Waverly St. Framingham, Ma 01702
3. Telephone Number: (508) 820 0606

E. COMPLAINT HISTORY:

Companion Complaints: (list docket numbers, allegations, status, and disposition)

Drug Store Prior History and outcome:

20021211ds036 - Board complaint - allegations: unprofessional conduct (JCE) pending board decision - 2/28/03

20032026ds060 - Consumer complaint - (Marsh) allegations: failure to adhere to standards of practice (JCE) - pending board decision 4/1/03

MDPH-Division of Health Professions Licensure
INVESTIGATION REPORT

Licensee Name:	Docket No.
New England Compounding Center And Barry Cadden	DS 03 055 PH 03 066

Pharmacist Cadden prior history and outcome:

19990330ph066 - Board complaint: allegations: violation of CMR 247 section 9.01(3) (JDC). Informal Reprimand issued for supplying prescriptions blanks to practitioners, dismissed 12/1/0/99

20021211ph042 - Board complaint - allegations: unprofessional conduct, (JCE) - pending board decision, 2/28/03

20030226ph070 - Consumer complaint - (Marsh) allegations: failure to adhere to standards of practice - (JCE) pending board decision, 4/11/03

- **Pending/Related Complaints:** (list docket numbers, allegations, status, and disposition)

See above as stated

Criminal Offender Records Information Check (CORI) been performed? ☐ Yes **X No**
Include certified copies of judgments

SECTION II: Interviews, Complainant Info & Index of Materials/Documents

A. INTERVIEWS CONDUCTED: List below and include labeled interview notes in case file

Individuals Interviewed (name/title)	When/Where? (dates/time of day)	Type Interview (in-person/phone)	Contact Information (phone, address, business)
1.			
2.			
3.			
4.			
5.			

B. WITNESSES NOT AVAILABLE FOR INTERVIEW: Document attempts in case file

Individuals	Contact Information (phone, address, business)	Attempt(s) to contact (dates, times)
1.		
2.		
3.		

MDPH-Division of Health Professions Licensure
INVESTIGATION REPORT

Licensee Name:	Docket No.
New England Compounding Center And Barry Cadden	DS 03 055 PH 03 066

C. COMPLAINANT INFORMATION:

A. NAME OF COMPLAINANT: Mass. Board of Registration in Pharmacy

B. ADDRESS: 239 Causeway St. Suite 500 - Boston, MA 02114

C. PHONE NO: (617) 727 9953 CELL PHONE: (n/a)

D. INDEX OF MATERIALS/DOCUMENTS: Label documents/materials as noted below in order of presentation in the file

ITEM A: Complaint
ITEM B: Record of standing
ITEM C: Complaint history
ITEM D: List of Concerns / DHHS/FDA
ITEM E: NECC response to allegations
ITEM F: Air Analysis
ITEM G: NECC P&P Procedures
ITEM H: NECC response to FDA
ITEM I: FDA Letter to Board
ITEM J: Copy of 2/20/2004 Compliance Inspection.

SECTION III: Investigation Summary

A. Allegation of Complaint: give nature code and summarize the allegations:

Complaints as referenced in docket numbers DS 03-055 and PH 03 066 were filed by the Mass. Board of Registration against New England Compounding Center, and Barry Cadden, Manager of record for the facility, based on the failure to adhere to standards of practice for compounding prescriptions. Specifically, the pharmacy and pharmacist engaged in unprofessional conduct as exhibited by; failing to follow guidelines, sterility procedures, record keeping requirements, batch records, failing to provide certificates of analysis, proof of sterility testing, Endotoxin test results, batch numbers and prescriptions upon request.

B. Setting Where Alleged Incident/Conduct Occurred:

1. Facility or Business Type: Pharmacy - Compounding Pharmacy
   Name: New England Compounding Center
   Address: 697 Waverly St. Framingham, Ma 01702
   Phone No: 508 820 0606
   Contact Person: Barry Cadden
   Contact's Title: Manager of Record

MDPH-Division of Health Professions Licensure
INVESTIGATION REPORT

Licensee Name:	Docket No.
New England Compounding Center And	DS 03 055
Barry Cadden	PH 03 066

2. Licensee's Supervisor (if applicable give name): not applicable
Phone No: N/A

C. Attorney of Record
1. Name of Attorney:

Attorney John Tamkin	617 964 2501
Attorney Jeff Gibbs	202 737 4288
Attorney Paul Cirel	617 371 1025
Hyman, Phelps, McNamara	202 737 5600

For FDA concerns:
Attorney Douglas B Farquhar 202 737 5600

2. Name of Firm:
3. Address:
4. Phone Nos.

D. Answer of Respondent (summarize licensee's response to allegations):

Licensee denied the allegations and has submitted copies of policy and procedures along with corrective measures.

E. Investigator's Activities and Findings:
Describe in narrative format - who, what, where, when, and why and include citations to laws and regulations when applicable to the case.

The Mass. Board of Registration in Pharmacy has filed a complaint against New England Compounding Center (NECC) and Barry Cadden, Manager of record, as it relates to the standards and procedures, sterility, record keeping, certificates of analysis, sterility testing, Endotoxin test results, compound formulations, and batch records for product compounded as such records could not be produced and matched up to dispensed prescriptions.

Based on a confidential report submitted on a Med. Watch form to the District Office of the Food and Drug Administration (FDA) in Stoneham, it is alleged that NECC compounded Betamethasone Repository Injection 6mg/ml. pursuant to patient specific prescriptions, and delivery to an unnamed medical facility where the medication was administered to patient(s). It is alleged that the patient(s) had an adverse event after the administration of this compounded drug. In both instances the drug was prepared by New England Compounding Center.

During the compounding and preparation process at NECC lot numbers were assigned to the product. Mr. Cadden could not produce an accountability of the product compounded. The FDA was concerned regarding a specific date the Batch of Betamethasone Repository 6mg/ml was compounded. The error was first reported in March 2002. The unnamed facility conducted sterility and Endotoxin tests on the product prepared by NECC, the results indicated a positive test for Endotoxin.

Licensee Name:	Docket No.
New England Compounding Center And	DS 03 055
Barry Cadden	PH 03 066

Mr. Cadden explained that at the time of preparation, lot numbers were assigned to each patient, however, upon request to review such documentation Mr. Cadden could not provide records for the lot number identified by FDA. Mr. Cadden stated while the lot number was generated, the medication was not dispensed. However, there was no notation to indicate such and, further no prescriptive records could be provided, nor could any certificates of analysis, Endotoxin test results, sterility test results, procedures on aseptic techniques or records indicating training of staff was provided.

When asked to describe his compounding process for the Betamethasone Repository Injection 6mg./ml. Mr. Cadden stated he used Sodium Carboxymethylcellulose, as an suspending agent . After the suspending agent was added the product was placed in the IV hood located in the IV room to cool for up to 4 hours. A sample is taken and sent to the test lab (Analytic Research Lab 840 Research Parkway, #546 Oklahoma City Oklahoma 73104.) Testing may take up to seven days, and during this time the product remained in the hood capped with foil.

Mr. Cadden also stated the medication was being administered via the epidural route, a non-approved route of administration. In response to this incident, NECC changed the suspending agent to Polyglycol.

CORRECTIVE MEASURES;

In February, 2003, Mr. Cadden responded to the allegations with corrective measures in February 2003 stating that he hired a consultant to develop policy and procedures. (Mr. Eric Brennan). All technicians are now certified and registered with the Board of Pharmacy. All staff receives training from Pharmacy Compounding Center of America (PCCA) in Texas after six month of employment. In addition:

1) All chemicals purchased are in date; beyond use dates are included on each formulation. All products are ordered from FDA registered facilities.
2) PCCA provides formulations for compounding.
3) Certificate of analysis for all chemicals are now kept on site.
4) Analytical tests results are obtained and kept on site.
5) Log sheets are current and up to date reflecting product name, active ingredients, expiration dates, manufacturer lot numbers, pharmacy lot numbers, name of patient, and Rx number. Expected yield will be included on all log sheets for each compounded product. All prescriptions can be traced back to a lot number thus enabling the pharmacist to trace product in the event of an adverse event or recall.
6) Policy and procedures are on site, and employees read and sign a statement of understanding.
7) Random samples are routinely collected and sent to an independent lab for sterility, and Endotoxin (pyrogenicity) testing. Remainder lots are placed in a quarantine area i.e.: refrigerator if needed, pending test results. Products of same lot are not re-tested in future. Samples are collected and microbial tests are completed to ensure the products are sterile. Each bulk lot of sterile end products must be tested for sterile Endotoxin, and fungal growth by an independent lab.
8) NECC has implemented an aseptic process validation protocol similar to USP 25-NF21 < 1211 (NECC-SOP 7.20).
9) When product becomes outdated, it is placed in a designated area until it can be destroyed.
10) NECC has obtained the services of a DEA reverse distributor.

Licensee Name: **Docket No.**

11) NECC dispenses and prepares products for compounding pursuant to a valid patient prescription obtained from a prescriber, and reduced to writing on an approved prescription blank.
12) In January 2003 NECC changed to a Class 10 Microenvironment for preparation of all sterile products / injectables. Autoclaves are used to sterilize products and vials.
13) NECC did conduct the recall requested by the FDA both in writing and by means of telephone communication on 2/14/03.
14) Sterilized vials are purchased from an outside vendor. Rubber stoppers are rinsed in sterile water to remove particulate matter and then autoclaved according to SOP.
15) SOP for weighing balances has been developed and printouts are attached to log sheets.
16) Formulation logs include examination of end product for closure, integrity, color, clarity, and presence of visible foreign particles.
17) Documentation of calibrations of a Baxa Repeater Pump and maintenance of all measuring equipment is now located in SOP and are in effect.
18) SOP's are in place for sterile and non-sterile compounded product.
19) SOP's are in place for complaints and for tracking of complaints.
20) All USP and NF guidelines are followed.
21) NECC uses NABP's Model Rules, adheres to CMR 247, FDA 795 (non- sterile products), 1206/797 (sterile products) and Chapter 460.200.

Describe documentation/facts that support allegations:

In April, 2002, the Board had the following concerns:

1) Pharmacy continues to reduce to writing orders on bulk purchase order forms and not on approved prescription blanks. An issue previously addressed with Mr. Cadden.
2) Batch logs are not initialed or signed by technicians preparing the compound.
3) Expiration dates are not current on the batch logs. (Mr. Cadden stated that the expirations dates upon receipt of the product were entered into the computer however, they were not updated upon filling of the prescriptions.)
4) On some occasions wholesalers would not furnish certificate of analysis.
5) Calculations performed by technicians were not documented on the prescription and no pharmacist verification documentation to ensure the calculations were accurate.
6) Prescriptions are not filed in a timely manner.
7) Perpetual inventory for control substances schedule II performed every 30 days.
8) Copies of DEA Licenses are not kept at the pharmacy, but at the licensee's home.
9) Copies of CMR 247 not on location, biennial inventory not available for review, technicians were not wearing name badges.
10) Pharmacy did not have a reverse distributor for recalled and / or out of date product.
11) Pharmacy had no written documentation that technicians review technician rules and regulations as they relate to CMR 247, or, any facility policy and procedure as they relate to compounding, or registration exams.

In October, 2002, Board had the following concerns: FDA investigators informed the Mass. Board of Pharmacy that a second incident involving NECC occurred. The compounded product was identified as Methyprednisolone Acetate.

MDPH-Division of Health Professions Licensure
INVESTIGATION REPORT

Licensee Name:	Docket No.
New England Compounding Center	DS 03 055
And	
Barry Cadden	PH 03 066

In February, 2003, the Board had the following concerns:

1) Batch logs are not initialed or signed by technicians preparing the compound.
2) Expiration dates are not current on the batch logs. (Mr. Cadden stated that the expiration dates upon receipt of the product were entered into the computer however, they were not updated when filling of the prescriptions.)
3) On some occasions wholesalers would not furnish certificate of analysis, sterility testing, Endotoxin test results, and batch numbers, and corresponding prescriptions could not be provided.
4) Prescriptions are not filed in a timely manner,
5) Perpetual inventory for control substances schedule II is performed every 30 days.

Describe any information learned or submitted that does not support the allegations:

Food and Drug Administration Investigators agreed that New England Compounding was not manufacturing any product.

Describe any information requested and not received:

All documentation requested from Mr. Cadden as part of this investigation has been provided.

Describe any exhibits not in case file (radiographs, tapes, etc.). Describe location and with whom.
N/A

List other state/federal or municipal agencies involved or also investigating this case and include contact information (name, address, telephone no.)

Food and Drug Administration – Stoneham, MA [redacted]; [redacted] – investigator, [redacted] compliance officer, [redacted] compliance officer, pharmacist.

F. In your opinion should case go to Medical Error Triage? ☐ Yes x☐ No
Explain:

G. Summary of alleged violations of regulation/statutes:

CMR 247 9.01 (3) - prescription pads
CMR 247 9.01 (14) - perpetual inventory
CMR 105 721.032 - prescription blanks
USP and ASHP guidelines

INVESTIGATOR SIGNATURE _____ **DATE** MAR 4 2004

SUPERVISOR SIGNATURE Patricia Romanti **DATE** 3/4/04

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MDPH-Division of Health Professions Licensure
INVESTIGATION REPORT

Licensee Name:	Docket No.
New England Compounding Center	DS 03 055
And	
Barry Cadden	PH 03 066

STAFF RECOMMENDATION: Pre-Board Staff Review Date:

Dismissal	XX	Formal Reprimand
Dismissal without prejudice		Censure
Dismissal with prejudice		Summary Suspension
No Violation		Suspension term:
Lack of Sufficient Evidence		
Advisory Letter		Probation term:
		Stayed Probation term:
Continuing Education		Revocation term:
Offer Voluntary Surrender		Non-disciplinary Agreement

Notes:
Based on this pharmacy's history as it relates to prior concerns of the Board agents since 1999, it is this investigator's opinion that a formal reprimand should be issued. At this time February 20,2004 a re-inspection of the pharmacy indicated that the corrective measures are in place and have been followed through as stated in Mr. Cadden's response to the Board.

****

BOARD'S Decision/Recommendation: Board Meeting Date:

Dismissal	Formal Reprimand
Dismissal without prejudice	Censure
Dismissal with prejudice	Summary Suspension
No Violation	Suspension term:
Lack of Sufficient Evidence	
Advisory Letter	Probation term:
Continuing Education	Stayed Probation term:
	Revocation term:
Offer Voluntary Surrender	

Notes:

MDPH-Division of Health Professions Licensure
INVESTIGATION REPORT

Licensee Name: Docket No.

Votes:

****

DISPOSITION OF CASE:

Refer to Board Counsel Date:

Refer to Prosecution Date:

Other

NEW ENGLAND COMPOUNDING CENTER **DS 2848**
697 WAVERLY ST. FRAMINGHAM, MASS

Manager of record: Barry Cadden PH 21239

Date of concern:	**CONCERN / COMPLAINT / STAFF ASSIGNMENT**
5/4/98	**APPLICATIOAN FOR NEW COMPOUNDING PHARMACY** with waivers assignment number SA PH 98 139. Board requests pharmacy changes name from pharmacy to center to prevent consumer confusion. Licensee Barry Cadden manager of pharmacy PH 21239. Has policy and procedures relating to compounding process guidelines, technician responsibilities, and calibration logs, various temp. Logs standard operation procedures for aseptic technique. Investigator: Leslie Doyle
4/16/99	PH.99-066 **Complaint** filed by Board of Registration in Pharmacy against New England Compounding Center in Framingham, Ma for alleged violations of CMR 247 Sec 9.01 (13) wherein a pharmacist or pharmacy department may not provide any practitioner with prescription blanks which refer to any pharmacist, pharmacy, pharmacy department. Investigator: James D. Coffey - dismissed with informal reprimand for supply prescription blanks to practitioner 12/1999
6/27/01	**SA PH 01 097 staff assignment** to investigate an incident report submitted by the Idaho Board of Pharmacy relating to NECC for soliciting business approved for drug products which should have been discontinued by the manufacture or may be unavailable. Discern whether the pharmacy regulations are being adhered to. An unapproved prescription form is attached. Completed inspection report dated 6/27/01 is also attached for review, Investigator: Leslie Doyle
4/10/02	**SA PH 02 092 staff assignment** to investigate and inspect NECC in Framingham in a joint inspection with FDA / Stoneham investigators who received a report pertaining to 2 adverse events which occurred to patients after receiving complaints from consumers. Investigator Leslie Doyle
4/18/02	Letter received from Nevada Board of Pharmacy as it relates to NECC selling drugs that are non-NDA approved products to physicians in Nevada.
10/2/02	Letter from pharmacist in NY [redacted] who is employed at a NY Hospital who has concerns about NECC in Framingham, Ma. and the dispensing of a compounded product: Methylprednisolone Acetate.

12/12/02	**Drug Store Complaint DS 03 036 and companion pharmacist complaint PH 03 042** - allegations of unprofessional conduct in the practice of pharmacy. Licensee stated that to the best of his knowledge the incident in question involves NECC faxing order sheets to prescribing physicians. Investigator: James Emery pending board 2/28/03
2/12/03	**Drug Store Complaint DS 03 055 and companion pharmacist complaint PH 03 066** - alleged failure to adhere to standards of practice. Investigator: Leslie Doyle - pending board 8/11/03
2/26/03	**Drug store Complaint DS 03 060 and companion pharmacist complaint PH 03 070** allegations failure to adhere to standards of practice, Investigator James Emery - pending board 4/11/03
2/20/03	Follow up inspection and site visit to ensure corrective measures are in place with Investigator James Emery and Leslie Doyle. Inspection report attached. Facility has Instituted corrective measures and provides evidence of follow through.

NEW ENGLAND COMPOUNDING CENTER
697 WAVERLY ST. FRAMINGHAM, MASS

(Using guidelines: ASHP vol. 57 (6-45) -2000 and USP 25 Chapter 1206 – current

CITATION / VIOLATION	CONCERNS
USP pg 2247 & ASHP RL 3.4 pg 1161	Inadequate documentation exists for equipment and supplies entering the product preparation area are Decontaminated
	2/20/04 - Re-inspection for compliance and assurance those corrective measures as stated in February 2003 were carried out. Associated compounding logs and batch reports were retrieved for the time period of 2/03, 6/03, 10/03, and 1/04. Investigators found the facility was in compliance.
USP pg 2235 & ASHP RL 3.6 pg 1162	Autoclave sterilization processes are suitable for the sterilization of drug product preparation equipment and components.
	2/20/04 - Re-inspection for compliance and assurance those corrective measures as stated in February 2003 were carried out. Associated compounding logs and batch reports were retrieved for the time period of 2/03, 6/03, 10/03, and 1/04. Investigators found the facility was in compliance.
USP pg 2236 & ASHP RL 3.7 pg 1162	Lack of documentation to verify that all critical processing parameters being used are appropriate that final products meet all standards
	2/20/04 - Re-inspection for compliance and assurance those corrective measures as stated in February 2003 were carried out. Associated compounding logs and batch reports were retrieved for the time period of 2/03, 6/03, 10/03, and 1/04. Investigators found the facility was in compliance.
USP pg 2236 & ASHP RL 3.12 pg 1163	Records do not state actual critical parameters used during processing. **Corrections noted 2/20/04**

USP pg 2243 & ASHP RL 3.4 pg 1161	Lack of documentation to verify that the autoclave itself is maintained and calibrated to perform its intended function. **Corrections noted 2/20/04**
USP pg 2235 & ASHP RL 3.6 pg 1162	Autoclave process used on bulk drug product does not have effect on stability or product specification. **2/20/04 - Re-inspection for compliance and assurance those corrective measures as stated in February 2003 were carried out. Associated compounding logs and batch reports were retrieved for the time period of 2/03, 6/03, 10/03, and 1/04. Investigators found the facility was in compliance.**
USP pg 2246	Inadequate documentation available for handling and disposition of reports of patient problems, complaints, adverse drug actions, drug product or device defects. **Corrections noted 2/20/04**
USP pg 2246	No written procedures for handling complaints nor is a complaint file maintained **Corrections noted 2/20/04**
ASHP RL 3.1 pg 1160	No written procedures available pertaining to performance of duties and process. **Corrections noted 2/20/04**
USP pg 2240 & ASHP RL 3.4 pg 1161	Equipment and supplies entering the product preparation area a decontaminated / cleaned to prevent Product Contamination. **2/20/04 - Re-inspection for compliance and assurance those corrective measures as stated in February 2003 were carried out. Associated compounding logs and batch reports were retrieved for the time period of 2/03, 6/03, 10/03, and 1/04. Investigators found the facility was in compliance.**
USP pg 2235 & ASHP RL 3.6 pg 1161	Transfer of bulk drug product and equipment from one room to another can not ensure that contamination is not occurring.

2/20/04 - RE-inspection for Compliance and assurance that corrective measures as stated in February 2003 are being followed through investigators found compliance. Associated compounding logs and batch reports were retrieved for the time period of 2/03, 6/03, 10/03 and 1/04.

USP pg 2235 & ASHP RL 3.6 pg 1161

Standards are not suitable for all drug products, components, drug substances including vials, and rubber stoppers to prevent contamination of finished product.

2/20/04 - Re-inspection for compliance and assurance those corrective measures as stated in February 2003 were carried out. Associated compounding logs and batch reports were retrieved for the time period of 2/03, 6/03, 10/03, and 1/04. Investigators found the facility was in compliance.

ASHP RL 3.10 pr 1162

Equipment used to measure the amount of ingredients / components are calibrated and maintained to perform their intended functions. Testing procedures and sampling procedures being performed for all drug products area representative of the lots/batches being tested.

2/20/04 - Re-inspection for compliance and assurance those corrective measures as stated in February 2003 were carried out. Associated compounding logs and batch reports were retrieved for the time period of 2/03, 6/03, 10/03, and 1/04. Investigators found the facility was in compliance.

USP pg 2235 & ASHP RL 3.6 pg 1161

Transfer of bulk drug product and equipment from the autoclave after it went through an autoclave Process from one room to another in which further preparation steps are performed in a laminar flow workbench is not introducing contamination into the finished product. All components including drug substances, vials and rubber stoppers, meet set standards making them suitable for their intended use. **Corrections noted 2/20/04**

ASHP RL 3.10 pg 1162

That for each preparation of a sterile product or batch of sterile products there has been appropriate laboratory determination of conformity with the purity, accuracy, sterility and non-pyrogenicity, in accordance with established written specifications and policies.

2/20/04 - Re-inspection for compliance and assurance those corrective measures as stated in February 2003 were carried out. Associated compounding logs and batch reports were

retrieved for the time period of 2/03, 6/03, 10/03, and 1/04. Investigators found the facility was in compliance.

ASHP RL 3.6 pg 1162

Preparation steps are being performed in a correct manner since batch record preparation instructions are lacking significant preparation steps which include mixing procedures. Final containers are capable of maintaining product integrity (i.e.: identity, strength, quality, and purity) throughout the shelf life of the product.

2/20/04 - Re-inspection for compliance and assurance those corrective measures as stated in February 2003 were carried out. Associated compounding logs and batch reports were retrieved for the time period of 2/03, 6/03, 10/03, and 1/04. Investigators found the facility was in compliance.

USP pg 2244 & ASHP RL 3.8 pg 1162

All drug products prepared and packaged at your site meet specifications and USP limits for the expiration dating period assigned. According to the documentation and your statements, all drug products are assigned an expiration date of sixty (60) days if they do not contain a preservative, three (3) months if they are not filtered, and six (6) months if they are filtered. No data was available for any of your products prepared at your firm to support this expiration date period.

2/20/04 - Re-inspection for compliance and assurance those corrective measures as stated in February 2003 were carried out. Associated compounding logs and batch reports were retrieved for the time period of 2/03, 6/03, 10/03, and 1/04. Investigators found the facility was in compliance.

ASHP RL 3.6 pg 1161

Components and process water are not contaminating finished products
Corrections noted 2/20/04

USP pg 2237 & ASHP RL 3.7 pg 1162

Personnel performing preparation steps are not contaminating the finished product Inadequate Documentation to verify that sterile drug products preparation meet standards.

2/20/04 - Re-inspection for compliance and assurance those corrective measures as stated in February 2003 were carried out. Associated compounding logs and batch reports were retrieved the time period of 2/03, 6/03, 10/03, and 1/04. Investigators found the facility was in compliance. Staff is gowned, capped, booted, and gloved when preparing all product

USP pg 2239 & ASHP RL 3.4 pg 1161	Workspaces are cleaned and sanitized to prevent contaminates. **2/20/04 - Re-inspection for compliance and assurance those corrective measures as stated in February 2003 were carried out. Associated compounding logs and batch reports were retrieved for the time period of 2/03, 6/03, 10/03, and 1/04. Investigators found the facility was in compliance.**
USP pg 2241 & ASHP RL 3.4 pg 1161	Environment in area where filling and closing operations are performed is adequate to prevent product contamination- pertaining to environmental monitoring in immediate are while product is exposed and prior to container closures. **2/20/04 - Re-inspection for compliance and assurance those corrective measures as stated in February 2003 were carried out. Associated compounding logs and batch reports were retrieved for the time period of 2/03, 6/03, 10/03, and 1/04. Investigators found the facility was in compliance.**

Concerns with no citations/violations available

- No data available for any products prepared as it relates to expiration date periods
- Calibration standards are not in place for equipment to measure amount of ingredients/ components
- Lack of testing procedures and sampling procedures being performed for all drug products
- Lack of batch record preparation to include insufficient preparation steps including mixing preparations
- Final containers lack integrity for maintaining product throughout shelf life
- Incomplete and lack of documentation as it relates to appropriate laboratory conformity for purity, strength, sterility, and non-pyrogenicity with written specification and processes.

2/20/04 - RE-inspection for Compliance and assurance that corrective measure as stated in February 2003 are being followed through investigators found compliance. Associated compounding logs and batch reports were retrieved for the time period of 2/03, 6/03, 10/03 and 1/04. Microsphere 10 system is in place and is a closed unit. Copy of the inspection report is attached to the complaint files.

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT OFFICE ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
One Montvale Avenue, 4th Floor Stoneham, MA 02180 [redacted]	10/24, 12/12&18/02, 1/14-15/03, 2/10/03
	FEI NUMBER 3003623877

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: Barry J. Cadden, Director of Pharmacy

FIRM NAME	STREET ADDRESS
New England Compounding Center	697 Waverly Street
CITY, STATE AND ZIP CODE Framingham, MA 01702	TYPE OF ESTABLISHMENT INSPECTED Pharmacy

DURING AN INSPECTION OF YOUR FIRM I OBSERVED:

The below observations pertain to drug products that personnel prepare at your firm for which you claim are sterile (for example, injections) and are prepared in anticipation of a prescription.

1. For the preparation of sterile drug products distributed by your firm (such as those intended for injection), there is no adequate documentation available to verify that they meet set standards (such as specifications and/or USP limits if applicable) at the time they are distributed or for the shelf life (expiration dating period) of these products. This includes the absence of documentation to verify the following:

A. Personnel performing preparation steps are not contaminating the finished products.

B. Workspaces are cleaned and sanitized to prevent product contamination.

C. Equipment and supplies entering the product preparation area are decontaminated/cleaned to prevent product contamination.

D. The environment in the area where the filling and closing operations are performed is adequate to prevent product contamination (this includes the lack of documentation pertaining to environmental monitoring in the immediate area while product is exposed to the environment, such as during filling and prior to container closure).

E. All autoclave sterilization processes are suitable for the sterilization of drug product preparation equipment and components (which includes vial stoppers and bulk product). Some examples are:

a. Lack of documentation to verify that all critical processing parameters and procedures being used are appropriate in ensuring that final products meet all standards (such as sterility); this includes, sterilization time, temperature, size and nature of load, and chamber loading configuration.

b. Records do not state the actual critical parameters used during processing.

c. Lack of documentation to verify that the autoclave itself is maintained and calibrated to perform its intended function.

d. The autoclave process used on bulk drug products does not have an effect on stability or product specifications.

F. The transfer of bulk drug product and equipment from the autoclave (after it went through an autoclave process) from one room to another room in which further preparation steps are performed in a laminar air flow workbench, is not introducing contamination into the finished product.

G. All components, including drug substances, vials, and rubber stoppers, meet set standards making them suitable for their intended use. This includes that components and process water are not contaminating finished products.

H. Equipment used to measure the amount of ingredients/components are calibrated and maintained to perform their intended function.

I. Testing procedures and sampling procedures being performed for all drug products are representative of the lots/batches being tested.

J. That for each preparation of a sterile product or batch of sterile products there has been appropriate laboratory determination of conformity with purity, strength, sterility, and non-pyrogenicity, in accordance with established written specifications and policies.

K. Preparation steps are being performed in a correct manner since batch record preparation instructions are lacking significant preparation steps, which includes mixing procedures.

L. Final containers are capable of maintaining product integrity (i.e. identity, strength, quality, and purity) throughout

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (Print or Type)	DATE ISSUED
	[redacted]		2/10/03 2/10/03

FORM FDA 483 (8/00) PREVIOUS EDITION OBSOLETE INSPECTIONAL OBSERVATIONS PAGE 1 OF 2 PAGES

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT OFFICE ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
One Montvale Avenue, 4th Floor Stoneham, MA 02180 [redacted]	10/24, 12/12&18/02, 1/14-15/03, 2/10/03
	FEI NUMBER 3003623877

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: Barry J. Cadden, Director of Pharmacy

FIRM NAME	STREET ADDRESS
New England Compounding Center	697 Waverly Street
CITY, STATE AND ZIP CODE Framingham, MA 01702	TYPE OF ESTABLISHMENT INSPECTED Pharmacy

the shelf life of the product.

M All drug products prepared and packaged at your site meet specifications and USP limits (if applicable) for the expiration dating period assigned. According to documentation and your statements, all drug products are assigned an expiration date of 60 days if they do not contain a preservative, three months if they are not filtered, and 6 months if they are filtered. No data was available for any of your products prepared at your firm to support these expiration date periods.

In addition, for all of the items above there were no written procedures available pertaining to the performance of these duties and processes.

2. There are no written procedures pertaining to the handling of complaints, nor does your firm maintain a complaint file.

3. There was no documentation available for the handling and disposition of reports of patient problems, complaints, adverse drug reactions, drug product or device defects, and other adverse events reported. For example, after a medical facility reported adverse events associated with lot 053]2002@16, your firm conducted a recall of injectable steroid products and implemented shorter expiration dates and use of pre-sterilized vials. You stated you have no documentation available pertaining to an investigation being performed for this and other related lots which shows that adequate follow-up action was taken.

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (Print or Type)	DATE ISSUED
	[redacted]		2/10/03 2/10/03

FORM FDA 483 (8/00) PREVIOUS EDITION OBSOLETE INSPECTIONAL OBSERVATIONS PAGE 2 OF 2 PAGES

New England Compounding Center
Framingham MA 01702
EI: 10/24/02-2/10/03 KMJ/DAD
Attachment# 11 Page 2

The observations of objectionable conditions and practices listed on the front of this form are reported:

1. Pursuant to Section 704(b) of the Federal Food, Drug and Cosmetic Act, or

2. To assist firms inspected in complying with the Acts and regulations enforced by the Food and Drug Administration.

Section 704(b) of the Federal Food, Drug, and Cosmetic Act (21 USC 374(b)) provides:

"Upon completion of any such inspection of a factory, warehouse, consulting laboratory, or other establishment, and prior to leaving the premises, the officer or employee making the inspection shall give to the owner, operator, or agent in charge a report in writing setting forth any conditions or practices observed by him which, in his judgement, indicate that any food, drug, device, or cosmetic in such establishment (1) consists in whole or in part of any filthy, putrid, or decomposed substance, or (2) has been prepared, packed, or held under insanitary conditions whereby it may have become contaminated with filth, or whereby it may have been rendered injurious to health. A copy of such report shall be sent promptly to the Secretary."

Footnotes
72 – 73, 82

Food and Drug Administration Establishment Inspection Report

Date Assigned: 12/17/2002 **Inspection Start Date:** 10/24/2002 **Inspection End Date:** 02/10/2003

Firm Name & Address: New England Compounding Center , 697 Waverly Street Framingham, MA 01720 US

Firm Mailing Address:

FEI: 3003623877 **JD/TA:** 13 **County:** MIDDLESEX **Est Size:** 0 - 24,999

Phone: [redacted] **District:** NWE-DO **Profiled:** No

Conveyance Type: **% Interstate:** **Inspectional Responsibility:**

Endorsement

SUMMARY: This inspection covered the firm's compounding processes for sterile injectable steroid products which included the following: methylprednisolone acetate and betamethasone repository (betamethasone sodium phosphate and betamethasone acetate). The MABP accompanied us during most of the inspection at the request of HFM-330.
The current inspection involved sampling of NECC products from within the New York and New England District areas. Sample results revealed that the firm has sterility and potency issues with injectable steroid suspensions (betamethasone repository USP and methylprednisolone acetate USP).

On 2/10/03, at the close of this inspection, an FDA-483, Inspectional Observations, was issued to Barry Cadden, R.Ph. The FDA 483 Observations pertained to the following: 1) inadequate documentation to verify sterile drug products distributed meet set standards (such as specifications and/or USP limits if applicable) or the assigned shelf life, 2) failure to maintain complaint files, including written procedures pertaining to the handling of complaints, and 3) lack of documentation for the reported adverse events associated with lot 05312002@16 of methylprednisolone acetate which includes handling and disposition of reports of patient problems, complaints, adverse drug reactions, and drug product or device defects.

(SEE CONTINUATION SHEET for Reason for Inspection, History, and Voluntary Corrections)

CLASSIFICATION: OAI; referral to Massachusetts State Board of Pharmacy. Recommend firm be prohibited from manufacturing until they can demonstrate ability to make product reproducibly and dependably. If state is unwilling to take action, recommend firm be enjoined for GMP deficiencies.

DISTRIBUTION:
Orig: CF
C/S &EIR: FMD-145, MA Bd Pharm thru Compl Br for FOI clearance
C/S &483: WSB, Souza
CC (C/S, EIR, 483, EXH & ATTCH): MCL, HFM-330 (Kathy Anderson)

Endorsement Location: NWE-DO CF

Inspector Name	Date & Time of Signature	Supervisor Name	Date & Time of Signature
[redacted]	03/07/2003 06:49 AM ET	[redacted]	03/07/2003 05:36 PM ET
	03/07/2003 06:49 AM ET		03/07/2003 05:30 PM ET
	03/06/2003 01:08 PM ET		ET
	03/06/2003 12:46 PM ET		ET
	03/06/2003 08:46 AM ET		ET
	03/05/2003 02:50 PM ET		ET

Food and Drug Administration Establishment Inspection Report

FEI:3003623877 **Inspection Start Date:** 10/24/2002 **Inspection End Date:** 02/10/2003

Firm Name & Address: New England Compounding Center , 697 Waverly Street Framingham, MA 01720 US

Related Firm FEI: **Name & Address of Related Firm:**

Registration Type

There are no Registration Types

Registration Dates

Establishment Type

M Manufacturer

M Manufacturer

Industry Code

60 Human and Animal Drugs

64 Human and Animal Drugs

District Use Code:

Food and Drug Administration Establishment Inspection Report

FEI: 3003623877 **Inspection Start Date:** 10/24/2002 **Inspection End Date:** 02/10/2003

Firm Name & Address: New England Compounding Center , 697 Waverly Street Framingham, MA 01720 US

Inspection Basis: Surveillance

Inspected Processes & District Decisions

PAC	Establishment Type	Products/ Process	MQSA	Reschedule Insp Date	Re-Inspection Priority	Inspection Conclusions
56D015	Manufacturer	64 L C K			Surveillance	Correction Indicated (CI)

Final Decision?	District Decision Date	District Decision Type	District Decision Made By	Org Name
Y	03/07/2003	Referred to State (RTS)	[redacted]	NWE-DRUGS

Remarks:

PAC	Establishment Type	Products/ Process	MQSA	Reschedule Insp Date	Re-Inspection Priority	Inspection Conclusions
56002	Manufacturer	64 L C K			Surveillance	Correction Indicated (CI)

Final Decision?	District Decision Date	District Decision Type	District Decision Made By	Org Name
Y	03/07/2003	Referred to State (RTS)	[redacted]	NWE-DRUGS

Remarks:

Food and Drug Administration Establishment Inspection Report

FEI: 3003623877 **Inspection Start Date:** 10/24/2002 **Inspection End Date:** 02/10/2003

Firm Name & Address: New England Compounding Center , 697 Waverly Street Framingham, MA 01720 US

Products Covered

Product Code	Est Type	Description	Additional Product Description
64 L C K 07	Manufacturer	Betamethasone Sodium Phosphate (Glucocorticoid); Human - Rx/Single Ingredient; Sterile Liquid	in amber vial
64 L C K 45	Manufacturer	Methylprednisolone Acetate (Glucocorticoid); Human - Rx/Single Ingredient; Sterile Liquid	in amber vial

Assignees Accomplishment Hours

Employee Name	Position Class	Hours Credited To	PAC	Establishment Type	Process	Hours
[redacted]	INV	NWE-DO	56D015	Manufacturer	64 L C K	200
	INV	NWE-DO	56D015	Manufacturer	64 L C K	35
	INV	NWE-DO	56002	Manufacturer	64 L C K	20
	INV	NWE-DO	56002	Manufacturer	64 L C K	15
					Total Hours:	270

Food and Drug Administration Establishment Inspection Report

FEI: 3003623877 **Inspection Start Date:** 10/24/2002 **Inspection End Date:** 02/10/2003

Firm Name & Address: New England Compounding Center , 697 Waverly Street Framingham, MA 01720 US

Inspection Result

EIR Location **Trips Num**
NWE-DO CF

Inspection Summary
REASON FOR INSPECTION: The investigation of New England Compounding Center (NECC) was conducted in response to an assignment (dated 8/2/02) received from HFM-330, Office of Compliance, Division of Prescription Drug Compliance and Surveillance, Center for Drug Evaluation and Research. The investigation was done in accordance with HFM-330 assignment/guidance and CPG 460.200 (Pharmacy Compounding). A limited inspection was performed which included covering aseptic processing procedures used at NECC. Sections of the current USP were used as a reference.
FACTS #332851.

The initial assignment requested an investigation to obtain information regarding three MedWatch reports associated with the use of methylprednisolone acetate preservative free 80mg/ml that was compounded by NECC in May of 2002. Per supervisory request, this assignment was changed to conduct an inspection during December 2002. The HFM-330 assignment requested answers to the following questions: 1) have any other patients experienced adverse events from the compounded product and 2) has the pharmacy conducted follow up to determine whether there is a problem with the compounded product.

HISTORY: The last FDA inspection of NECC was in April 2002. The inspection was classified VAI and a FDA-483 (List of Observations) was issued to Mr. Cadden citing sterility issues and lack of lot accountability. The practices that were cited on the previous FDA 483 were not in place and therefore the correction of these items was not an issue.

VOLUNTARY CORRECTIONS: n/a

Food and Drug Administration Establishment Inspection Report

FEI: 3003623877 **Inspection Start Date:** 10/24/2002 **Inspection End Date:** 02/10/2003

Firm Name & Address: New England Compounding Center , 697 Waverly Street Framingham, MA 01720 US

IB Suggested Actions

Action	Remarks

Referrals

Org Name	Mail Code	Remarks

Refusals

Inspection Refusals:

Samples Collected

Sample Number
167876
167877
169126
169127
169128
169129
169130
169131
169132
169133
208553

Recall Numbers

Recall Number

Related Complaints

Consumer Complaint Number

FDA 483 Responses

483 Issued?: Y **483 Location:** NWE-DO CF

Response Type	Response Mode	Response Date	Response Summary
Further review needed	Letter	02/26/2003	Response outlined corrective actions; referred to MA State Bd of Pharmacy.

Footnotes
49 – 65, 83

New England Compounding Center | FEI# 3003623877
697 Waverly Street | FACTS #332851 | EI Start: 10/24/02
Framingham, MA 01702 | KMJ/DAD | EI End: 2/10/03

SUMMARY

The investigation of New England Compounding Center (NECC) was conducted in response to an assignment (dated 8/2/02) received from HFM-330, Office of Compliance, Division of Prescription Drug Compliance and Surveillance, Center for Drug Evaluation and Research. The investigation was done in accordance with HFM-330 assignment/guidance and CPG 460.200 (Pharmacy Compounding). A limited inspection was performed which included covering aseptic processing procedures used at NECC. Sections of the current USP were used as a reference.

The initial assignment requested an investigation to obtain information regarding three MedWatch reports associated with the use of methylprednisolone acetate preservative free 80mg/ml that was compounded by NECC in May of 2002. Per supervisory request, this assignment was changed to conduct an inspection during December 2002. The HFM-330 assignment requested answers to the following questions: 1) have any other patients experienced adverse events from the compounded product and 2) has the pharmacy conducted follow up to determine whether there is a problem with the compounded product.

The last FDA inspection of NECC was in April 2002. The inspection was classified VAI and a FDA-483 (List of Observations) was issued to Mr. Cadden citing sterility issues and lack of lot accountability. The practices that were cited on the previous FDA 483 were not in place and therefore the correction of these items was not an issue.

On 10/24/02, Investigator [redacted] showed credentials, and issued an FDA 482, Notice of Inspection (including the attachment Resources for FDA Regulated Businesses), to Barry J. Cadden, Owner and Director of Pharmacy. On 10/24/02 Inv. [redacted] was accompanied by [redacted] of the Massachusetts Board of Pharmacy (MABP). On 12/12/02 FDA Credentials were shown, and a second FDA 482 was issued to Mr. Cadden by Investigators [redacted]. On 12/12/02 Inv. [redacted] were accompanied by [redacted] Investigator, and [redacted] Quality Assurance Surveyor, from the MABP. On 12/18/02 Investigators [redacted] returned to the firm accompanied by [redacted]. On 1/14/03 Inv. [redacted] showed credentials, and issued an FDA 482 to Mr. Cadden for the purpose of sample collection. On 1/15/03 Inv. [redacted] showed credentials, and issued another FDA 482 to [redacted] Educational Coordinator, for the purpose of picking up a sample of vial caps. On 2/10/03 Inv. [redacted] showed credentials, and they issued another FDA 482, since they had not been at the firm for about three weeks.

This inspection covered the firm's compounding processes for sterile injectable steroid products which included the following: methylprednisolone acetate and betamethasone repository (betamethasone sodium phosphate and betamethasone acetate). The MABP accompanied us during most of the inspection at the request of HFM-330.

New England Compounding Center		FEI# 3003623877
697 Waverly Street	FACTS #332851	EI Start: 10/24/02
Framingham, MA 01702	KMJ/DAD	EI End: 2/10/03

The current inspection involved sampling of NECC products from within the New York and New England District areas. Sample results revealed that the firm has potency issues with injectable steroid suspensions (betamethasone repository USP and methylprednisolone acetate USP).

On 2/10/03, at the close of this inspection, an FDA-483, Inspectional Observations, was issued to Barry Cadden, R.Ph. The FDA 483 Observations pertained to the following: 1) inadequate documentation to verify sterile drug products distributed meet set standards (such as specifications and/or USP limits if applicable) or the assigned shelf life, 2) failure to maintain complaint files, including written procedures pertaining to the handling of complaints, and 3) lack of documentation for the reported adverse events associated with lot 05312002@16 of methylprednisolone acetate which includes handling and disposition of reports of patient problems, complaints, adverse drug reactions, and drug product or device defects.

ADMINISTRATIVE DATA

Post inspection correspondence should be sent to Barry Cadden R.Ph., Director of Pharmacy, at the below address.

Inspected Firm:	New England Compounding Center
Location:	697 Waverly Street Framingham, MA 01702
Phone:	[redacted]
FAX:	
Mailing Address:	[redacted] Framingham, MA 01702
Dates of Inspection:	10/24/02, 12/12&18/02, 1/14-15/02, 2/10/03
Days in the Facility:	6
Participants:	[redacted] Investigator , Investigator

The EIR was written by [redacted]

FIRM INFORMATION

Pertaining to key firm personnel and their responsibilities no significant changes were made since the previous April 2002 inspection (see April 2002 EIR).

NECC holds a restricted license in the state of Massachusetts to operate as a compounding pharmacy. Essentially, MABP permits NECC to dispense only compounded pharmaceutical products. This is the second joint FDA and MABP investigation of the firm; the first was in April 2002 and was also a CDER assignment initiated by MedWatch complaints about the firm's betamethasone repository injectable

product. Please refer to the April 2002 EIR for the firm's hours and organizational structure. The MABP was present during the April 2002 investigation at the request of the FDA NWE-DO office per HFM-330 assignment.

On April 16, 2002 an FDA-483 was issued to Mr. Cadden citing sterility issues pertaining to the transfilling practices for betamethasone repository injection. Lot accountability was also cited for incomplete computerized record keeping of generated lot numbers. Mr. Cadden stated there is no lag in the transfilling time as noted in the 4/16/02 FDA-483. We were unable to verify this since compounding was not observed during this inspection. This inspection was classified VAI. No regulatory activities occurred as a result of the April 2002 inspection.

Since the April 2002 inspection, there have been significant changes to NECC's operations. One change is the acquisition of space previously occupied by a neighboring store. This space approximately doubled the firm's square footage which is currently being used for office space and a reception area. Mr. Cadden stated he now employs approximately twelve people in the following roles: 2 Pharmacists, 4 Pharmacy Technicians, 1 Bookkeeper, 2 Customer Service, 1 Receptionist and 2 Salespeople. He stated that the firm's employees make calls to out-of-state physicians and medical facilities and also maintain a web site.

Another change since the April 2002 inspection is the renovation of a previous reception area to accommodate the firm's new Class 10 hood. At the FDA inspectional closeout on 2/10/03, it was confirmed that the new hood is installed and certified. Mr. Cadden stated the new hood is not in use yet while he is awaiting the approval of the MABP.

NECC is planning on marketing and selling compounded products in all 50 U.S. states per Mr. Cadden. He stated he is in the process of applying to each state in order to do so. Currently he estimated he has permission to do so from approximately 13 states, though he could not recall which specific states. Mr. Cadden stated his firm employs individuals that telephone and/or send correspondence to prospective customers (physicians and medical facilities) found on the internet or in telephone books. He stated this is done to find prospective in-state and out-of-state customers. He also stated that he intends to have a representative from his firm travel the state of Massachusetts to promote the firm's services to potential customers. The firm also maintains a web site which advertises the firm's services and contains downloadable order forms. Mr. Cadden stated the NECC web site does not accept orders on-line.

COORDINATION WITH MASSACHUSETTS STATE BOARD OF PHARMACY

The Massachusetts Board of Pharmacy (MABP) provided three representatives who were each present intermittently throughout the inspection. The representatives were [redacted] Supervisory Investigator, [redacted] Investigator, and [redacted]

Quality Assurance Surveyor. To facilitate the sharing of information with MABP, one of the MedWatch complainants was contacted regarding directly reporting the adverse events to the MABP. MABP representatives were present throughout the majority of the inspection, which further facilitated MABP and FDA communications.
In early 2002 the MABP designated a committee to formulate compounding regulations for the State. Currently these regulations are under review by MABP. MABP anticipates implementing these new regulations sometime in 2003. Mr. Cadden is a member of the committee assigned by MABP.

Correspondence to the MABP should be sent to the following address:

The Commonwealth of Massachusetts
Division of Professional Licensure
Office of Investigations
[redacted]

MEDWATCH COMPLAINTS

This investigation was conducted per the HFM-330 assignment issued to the New England District Office. The assignment requested the collection of information and samples of NECC products in association with MedWatch complaints. Three MedWatch reports were received by the FDA detailing adverse events that occurred in two patients in July 2002 at the (b)(6), (b)(7)(C). See **Attachment #1** for the HFM-330 assignment and three MedWatch reports. In the MedWatch reports, the complainant attributed the adverse reactions to a compounded methylprednisolone acetate preservative-free 80mg/ml injectable prepared by NECC in May 2002. The MedWatch complaints were reported by a physician and the Chief Pharmacist at (b)(6), (b)(7). The Chief Pharmacist and Quality Supervisor from (b)(6) were both contacted regarding the MedWatch reports and events surrounding the adverse reactions.

On 9/30/02, [redacted] spoke with the Chief Pharmacist (b)(6), (b)(7)(C). He stated that after the adverse reactions occurred, he instructed his staff to remove all the methylprednisolone acetate injectable with the affected lot number from the hospital floors. The collected vials were then turned over to the hospital's Quality Assurance personnel. The MedWatch report from the pharmacist stated samples were available.

On 9/4/02, 11/1/02 & 3/3/03 [redacted] spoke with (b)(6), (b)(7)(C), Quality Supervisor at (b)(6), (b)(7). On 9/4/02, [redacted] confirmed with (b)(6), (b)(7)(C) that samples were available. (b)(6), (b)(7)(C) stated that she had received the unused vials from the pharmacy department. Arrangements were made with the FDA New York District to collect the sample vials (b)(6), (b)(7)

(b) (6), (b) (7)(C) was able to describe the adverse events and surrounding incidents. She stated that both patients were given injections on (b) (6), (b) from the same lot (05312002@16) and both experienced pain and headache and were hospitalized with meningitis-like symptoms. Both patients received antibiotic therapy. Cultures of both patients' cerebrospinal fluid (CSF) were negative. Since both patients were on antibiotic therapy, the CSF cultures would be negative regardless of microbial growth prior to treatment. (b) (6), (b) (7)(C) did not have a hard copy of the CSF results. Both patients fully recovered. (b) (6), (b) (7)(C) confirmed the route of administration for both patients was intrathecal. One injection was intended as intrathecal and the other was unintended intrathecal (misplacement of needle into an unintended adjacent space).

One of the MedWatch reports stated the vials tested positive for gram negative organisms. Attached as **Exhibit #1** is the fax from (b) (6), (b) (7)(C) reporting results of the vial testing performed by (b) (6), (b) (7). The lab results show initially there was growth (gram negative rods), but after 8 weeks incubation there was no growth seen. (b) (6), (b) (7)(C) stated she believes the vial tested was from lot 05312002@16 and that the lab results are under one of the patient's names, but she believes it was the vial tested, not patient fluids (ie., not cerebrospinal fluid). Since they are single-dose vials, the actual vials used on the affected patients were discarded and could not be located.

When asked about actions taken by (b) (6), (b) (7) (b) (6), (b) (7)(C) stated she first contacted Mr. Cadden at NECC to make him aware of the adverse events. She stated she spoke with Mr. Cadden on/about 7/23/02. She stated she does not believe (b) (6) returned any of the vials to NECC. She believes they were all retained for FDA sampling and hospital investigative purposes. After the adverse events occurred, a hospital committee (including infectious disease and anesthesiology) looked into possible causes and determined, for lack of another answer, that the adverse events were caused by the compounded product from NECC.

SAMPLE COLLECTION BY FDA NYK DISTRICT: SEPTEMBER 9, 2002

A sample (FACTS 193610) was collected on 9/12/2002 by the New York District. The sample consisted of sixteen (16) vials of methylprednisolone acetate preservative-free (80mg/ml) injectable with "same lot number suspected for causing adverse reactions" in MedWatch reports. The sample was sent to FDA NRL for sterility and endotoxin testing. NRL was unable to perform the sample analysis until 4 days after the compounded product's expiration date. See **Attachment #2** for the collection report.

NOTE: The NRL reported the vials collected at (b) were from lot 051902@15, a different lot than the MedWatch reports. A NWE-DO Compliance Officer spoke with (b) (6), (b) (7), Quality Supervisor at (b) on 12/12/02. (b) (6), (b) (7) was surprised that the lot sampled by FDA at (b) was different than the lot indicated in the MedWatch reports. This issue was not resolved in their phone conversation.

On 12/11/02, the NRL reported positive results for sterility (gram negative organisms). On 12/12/02 Investigators [redacted] visited the firm to notify Mr. Cadden of

the positive sterility results found upon analysis of his compounded product (see below for full description of firm visit).

On 12/18/02, NRL reported that the organisms were identified as *Burkholderia cepacia* and *Sphinogomonas paucimobilis*. The following is an NRL Pharmaceutical Microbiologist's description of the organisms found in sample 193610:

"Description of each bacterium:

Burkholderia cepacia- Burkholderia are aerobic, non-spore-forming, gram-negative rods which are straight or curved. This type of bacteria are environmental organisms found in water, in soil, and on plants including fruits and vegetables."Because of their ability to survive in aqueous environments, these organisms have become particularly problematic in the hospital environment". "The genus Burkholderia contains two organisms frequently encountered as human pathogens, B. pseudomallei and B. cepacia"."B. c. is well recognized as a nosocomial pathogen causing infections associated with contaminated equipment, medications, and disinfectants including povidone-iodine and benzalkonium chloride". "B.c. is emerging as an important pathogen in two patient populations with genetic diseases, Cystic fibrosis, and chronic granulomatous disease"

Sphinogomonas paucimobilis- This group of bacteria is also an aerobic non spore forming , gram –negative rod. "The new genus Spingomonas was created for the organism formerly known as Pseudomonas paucimobilis and CDC IIk-1. The genus Sphingomonas presently contain 16 species, but only S.paucimobilis , which is designated the type species, is important clinically. Colonies grown on blood agar medium are yellow pigmented and slowly growing, with only small colonies observed after 24 hr of incubation. S.a. is widely distributed in the environment, including water, and has been isolated from a variety of clinical specimens, including blood, cerebrospinal fluid, peritoneal fluid, urine, wounds, vagina, and cervix and from hospital environment"

The source of the reference information was obtained from the Manual of Clinical Microbiology, 7th edition, 1999, published by the American Society for Microbiology".

Please refer to the following table for a description of NYK district samples collected and the subsequent NRL results.

SAMPLE	PRODUCT	LOT	QTY	Exp	Results
193610	Methylpredisolone AC (PF) 80MG/ML INJ	05192002@15	16	11/15/02	1/14= *Sphingomonas paucimonas* 4/14= *Burkholderia cepacia*

VISIT TO FIRM: OCTOBER 24, 2002

MABP Supervisory Investigator [redacted] accompanied [redacted] to the firm. Ms. [redacted] presented Mr. Cadden with a formal request for information. At that time she

informed Mr. Cadden that a copy of his response would be provided to the FDA. Please see **Exhibit #2** for the State's request for information and NECC written response.

Mr. Cadden stated he was telephoned by an employee from (b)(6) to notify him of the adverse reactions that were reported to MedWatch. He did not have the employee name, but did email that information to me the following day (**Exhibit #3**). (b)(6), (b)(7)(C) Quality Supervisor at (b)(6) notified Mr. Cadden about the adverse reactions associated with methylprednisolone acetate. Mr. Cadden stated (b)(6), (b)(7)(C) told him the adverse reactions were due to "administration errors" since the injections were administered intrathecally. The medication is not FDA approved for intrathecal administration. Mr. Cadden stated that the hospital had returned vials of the affected product to the firm and that NECC sent a sample of the returned product to its contract laboratory (Analytical Research Laboratories, Oklahoma City, OK (ARL) for testing. I viewed the laboratory results (received by lab on 8/20/02 and reported on 8/22/02). The results reported on 8/22/02 hard copy were negative for "endotoxin content and microbial contamination". I then viewed the initial ARL results (received by lab on 6/19/02 and reported on 6/20/02) for the affected lot, 05312002@16, which were negative for "endotoxin content and microbial contamination". See **Exhibit #4** for supporting documentation.

The following information was also obtained from Mr. Cadden:

1) Random sampling for finished compounds is as follows: for lots with small volume vials, 2-3 vials are tested and for lots of larger volume vials (ie., 10ml) 1 vial is tested for sterility and endotoxins.
2) NECC is still closed on Saturday and Sunday, but Mr. Cadden stated he often comes to work on Saturdays to make sterile compounds. Mrs. Cadden still works two to three days per week in an administrative role only.
3) Regarding the processing of sterile suspension injectable steroids: The compounding occurs in the "Clean Room". Once compounded, the suspension (in a beaker) is covered with 3 layers of aluminum foil, brought through the ante-room to the main compounding area and autoclaved. The suspension is then brought back through the ante-room into the "Clean Room". The suspension is brought to room temperature on a magnetic stirrer (approximately 2-4 hours) then the suspension is transferred to vials (various sizes) with a Baxter Repeater Pump. Mr. Cadden stated the bulk suspension is sterilized (versus sterilization in final vial container) because the properties of the suspension would not allow it to resuspend in the vials and the particle size would be too large. The steroid compounding formulas from Professional Compounding Centers of America, Houston, TX (PCCA) instruct him to compound the products in this way. Suspensions must be autoclaved since they cannot be filtered through a 0.22μ filter due to particle size.

[redacted] told Mr. Cadden that MABP discourages the use of "as directed" instructions on patient prescription labeling and that stock sold as "For Office Use Only" was not allowed in the state of Massachusetts unless the firm obtained a special permit.

New England Compounding Center | FEI# 3003623877
697 Waverly Street | FACTS #332851 | EI Start: 10/24/02
Framingham, MA 01702 | KMJ/DAD | EI End: 2/10/03

VISIT TO FIRM: DECEMBER 12, 2002

On 12/11/02, NRL informed NWE-DO that the sterility results for sample 193610 showed a presumptive positive for four (4) of fourteen (14) vials. At that time it became a priority to visit NECC to inform Mr. Cadden of the results and determine what his intentions would be regarding the compounded product. On 12/12/02, Inv. Joyce and DeWoskin went to NECC and informed Mr. Cadden of these results. Mr. Emery and Mr. Chaput from the MABP were present. Mr. Cadden stated that NECC had conducted a recall of the product in August 2002 (without FDA knowledge) after the adverse reactions were reported to NECC by the MedWatch complainant hospital. Mr. Cadden did not share this recall information with the FDA at the October 2002 visit to NECC. He stated recall notification to customers was done via telephone calls. The only record of the recall process was a three page table listing customer names, returned product and lot numbers. Recall information was requested per NWE-DO Recall Coordinator guidance.

Mr. Cadden confirmed prior to the recall he was using 6 month expiration dates for sterile products with preservatives and was sterilizing the vials himself at NECC. He stated he conducted a recall after receiving the complaint from (b)(6) in July 2002. He stated he received 500-600 vials back from customers as a result of the recall. He retested one (1) of these vials for sterility and endotoxin and the results were negative. Mr. Cadden showed us ARL #24399 results (refer to Exh. #4, pages 3&4). I asked Mr. Cadden if he thought of testing a more representative quantity from the returned product (ie., not just one vial), but he stated he only tested one vial. Mr. Cadden stated the corrections he has made since the complaint from (b)(6) include the following actions: 1) expiration date was decreased from 6 months to 60 days for preservative free products, and 2) utilization of a contract facility (Eagle-Picher) to pre-sterilize vials for use in sterile products. See **Exhibit #5** for information from Eagle-Picher Industries, Inc. website (Miami, OK).

Mr. Cadden stated he had not received any other complaints associated with the use of NECC compounded sterile steroid injectables. Representative testing for sterility and endotoxin was discussed with Mr. Cadden. We explained to Mr. Cadden that the USP contains guidance on sample sizes in relation to lot quantities. We also discussed validation and verification of testing procedures performed by contract laboratories.

While at the firm, samples were collected of methylprednisolone acetate preservative-free (PF) injectable and betamethasone repository injectable. After seeking supervisory guidance, I collected 20 x 1 ml vials of methylprednisolone acetate PF (80mg/ml) and 10 x 5ml vials of betamethasone repository (6mg/ml betamethasone repository = 3mg betamethasone sodium phosphate + 3mg betamethasone acetate). These compounds were chosen because they were associated with the current and April 2002 MedWatch reports. Both products are sterile suspension injectable steroids and are compounded by similar methods according to Mr. Cadden. See **Attachment #3, 4, & 5** for the FDA-463a (Affadavit), FDA-484 (Receipt for Samples), and collection reports.

New England Compounding Center
697 Waverly Street
Framingham, MA 01702

FACTS #332851
KMJ/DAD

FEI# 3003623877
EI Start: 10/24/02
EI End: 2/10/03

Please refer to the following table for a description of samples collected on this date and the subsequent NRL results.

SAMPLE	PRODUCT	LOT	QTY	Exp	Results
169126	Methylprednisolone AC (PF) 80 mg/ml x 1 ml	11262002@4	20	1/25/03	Assay= Within Range
169127	Betamethasone Repository (PF) 6mg/ml x 5ml (BSP+BA)	11302002@1	10	1/29/03	Assay= Subpotent BSP 77.4 (O); 74.6 (C/A) BA 71.6 (O); 71.0 (C/A)

VISIT TO FIRM: DECEMBER 18, 2002

A visit to the firm was conducted to request information regarding NECC recall procedures and collect samples. After conferring with NRL for sampling requirements, it was decided that further samples were necessary from NECC. See **Attachment # 6, 7 & 8** for the FDA-463a (Affadavit), FDA-484 (Receipt for Samples), and collection reports. Please refer to the following table for a description of samples collected on this date and the subsequent NRL results.

SAMPLE	PRODUCT	LOT	QTY	Exp	Results
169128	Methylprednisolone AC (PF) 40 mg/ml x 1 ml	11262002@5	50	1/10/03	Sterility= Negative Endotoxin- "not performed" Assay= Superpotent 131.4 (O) & 133.1% (C/A)
169129	**Betamethasone Repository 6mg/ml x 2 ml**	12102002@11	50	6/8/03	**Sterility= Negative Endotoxin= Negative Assay- subpotent BSP 67.0 (O); 62.0 (C/A) BA 59.8 (O); 58.7 (C/A)**
169130	Methylprednisolone AC (PF) 80 mg/ml x 1 ml	11262002@4	50	1/25/03	Sterility= Negative Endotoxin= Negative
169131	Triamcinolone Acetonide 40 mg/ml x 5 ml	112020002@8	34	2/18/03	Sterility= Negative Endotoxin "not performed"
169132	Prochlorperazine Edisylate 5 mg/ml x 10 ml	11112002@11	18	2/9/03	Sterility= Negative Endotoxin "not performed"
169133	Saline PF 10% Injectable x 15 ml	12122002@14	5	3/12/03	Sterility= Negative Endotoxin= "not performed"
208553	Betamethasone Repository (PF) 6mg/ml x 2ml	11302002@1	50	1/29/03	Sterility= Negative Endotoxin= "not performed"

1. PF= Preservative Free (for some products, NECC makes product both with and without preservative)
2. Betamethasone Repository= Betamethasone Sodium Phosphate & Betamethasone Acetate.

The following items were also discussed with Mr. Cadden:

1) Sampling of compounded products by NECC: The firm's sampling procedures were again discussed with Mr. Cadden. He stated he used the recommendations of his contract laboratory (ARL). I discussed with Mr. Cadden the USP recommendations for testing of sterile products. Mr. Cadden stated he would look at these recommendations and reconsider his testing procedures. A copy of the firm's sample log to ARL is attached as **Exhibit #5**.
2) Environmental Monitoring of "Clean Room": While discussing the firm's "clean room", Mr. Cadden stated that he has his laminar flow hood serviced yearly,

which includes HEPA filter testing (and replacement as necessary). I asked Mr. Cadden if he would know if the HEPA filter needed to be changed between yearly inspections and he stated no. I discussed with Mr. Cadden the impact that could have by possibly compromising the sterility of his product. I recommended NECC initially evaluate the life span of their HEPA filters (via more frequent monitoring) and compose a testing plan around that evaluation. Mr. Cadden stated that the firm changes the pre-filters every 4-6 weeks to prolong the life of the HEPA filter. Mr. Cadden stated another component of his yearly testing of the clean room is air sampling. I recommended Mr. Cadden consider expanding his environmental monitoring to include surface and wall sampling. I suggested guidance resources such as the USP.

3) Sterile compound preparation:
   a. Mr. Cadden stated that he uses a new set of disposable tubing for the Baxter Repeater Pump for each lot that is compounded.
   b. When asked what other sterile compounds are made by the firm, Mr. Cadden stated if he was able to filter the product that he would make the compound.
   c. Mr. Cadden stated the water source for sterile products comes from 1000 ml bags of Sterile Water for Injection.
   d. Mr. Cadden stated that NECC started to compound Prochlorperazine (Compazine) Injectable 2-3 weeks prior when he was able to access the bulk product.
   e. Mr. Cadden stated the firm does not dispense any medication to clients for office stock use. He stated that it would be a possibility in the future if Massachusetts state laws changed and allowed this of compounding pharmacies.
   f. [redacted] requested of Mr. Cadden the opportunity to observe production of sterile products in the very near future depending on his compounding schedule. On 12/23/02, [redacted] spoke with Mrs. Cadden who stated that compounding would not resume until after the start of the New Year since business was slow around the holidays.
   g. A copy of the NECC "Policies and Procedures for Compounding Sterile Products" and "Aseptic Compounding Policies and Procedures Manual" (SOP's) are attached as **Exhibit # 7 & 8**.

4) Recall Procedures:
   a. Health risk analysis: While discussing the lots made before August 2002 that were distributed with a 6 month expiration date, I asked Mr. Cadden if he had any intentions of recalling those products also since those products will continue to have expiration dates through February 2003. Mr. Cadden stated he did not have any intention of recalling products other than the steroid products recalled in August 2002. The firm's recall procedures in August 2003 consisted of calling clients who received the 05312002@16 lot of methylprednisolone and asking them to return any steroid product they had in stock. This means that clients who received lots other than the 05312002@16 were not notified of the recall or

possible problems with the products and will likely use those products until the expiration date of 6 months.

b. Mrs. Cadden stated she notified customers of the recall by telephone. We restated the information needed by FDA to process the recall. Please see the heading "Recall Information" for the information provided by NECC.
c. The returned products from the recall were still at NECC. Two large boxes were examined by [redacted] Lot numbers and product names were identifiable and it was confirmed that they were the products intended for the recall.
d. A copy of a FDA Talk Paper from 11/15/02 was given to Mr. Cadden and is attached as **Attachment #9**. This reference described current regulatory actions taken against compounding pharmacies.

VISIT TO FIRM: JANUARY 14, 2003 this section written by [redacted]

On 1/14/03, I [redacted] went to NECC. At the time of my arrival I showed my credentials and issued an FDA 482 to Barry Cadden. The purpose of this visit was to pick up a sample of sterilized vial stoppers and sterilized vials. The vial stoppers Mr. Cadden stated are bought pre-sterilized from Eagle Picher Environmental. Mr. Cadden provided CSO [redacted] with a sealed bag containing 100 vials from Eagle Picher Environmental which was submitted to Northeastern Regional Laboratory (NRL) for sterility and endotoxin testing. These vials are assigned Sample Number 167876. Also on this same date Mr. Cadden provided a sealed bag of vial stoppers which he stated he autoclaved. However, when I returned to the office, I noticed a tear in the bag; and therefore decided not to submit this sample. Instead I decided to go to NECC the following day for a new sample. When the tear was noticed I called the firm and notified [redacted] the Educational Coordinator, that I would be returning on 1/15/03 to collect some more autoclaved stoppers.

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When I was at the firm on 1/14/03 Barry Cadden notified me that his lawyer ([redacted] Massachusetts – phone 617-964-2501) instructed him to tell me that he would provide me samples, but if I had any other requests or questions pertaining to any of their procedures and compounding activities, I was to put my requests or questions in writing. Mr. Cadden stated he would then submit my requests to his lawyer for review, and then get back to me. At the time I was talking to Mr. Cadden I requested the address and name of customers who received lot 05312002@16, methylprednisolone 80mg/ml injection which is a lot number of product that stated he told people to return to NECC due to a potential problem, when I returned to the office I sent Mr. Cadden an e-mail repeating this request. As of 2/10/03, the date that the FDA 483 was issued, a response to this e-mail request had not been received.

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VISIT TO FIRM: JANUARY 15, 2003 (this section written by [redacted]

On 1/15/03, I [redacted] returned to NECC for the purpose of collecting a sample of sterilized vial rubber stoppers. I showed my credentials, and issued an FDA

New England Compounding Center
697 Waverly Street
Framingham, MA 01702

FACTS #332851
KMJ/DAD

FEI# 3003623877
EI Start: 10/24/02
EI End: 2/10/03

482 to [redacted] Educational Coordinator. [redacted] said Mr. Cadden was at the facility but not available. At this time she provided me a sample of vial stoppers in a sealed bag which she stated were autoclaved within the last day. I observed that there were water droplets in this bag with the stoppers and that they were making water stains on one part of the white packaging material of the autoclave bag. I submitted these vial stoppers to NRL as Sample #167877. After I was provided the sample by [redacted] left the firm.

Please refer to the following table for a description of samples collected January 14-15, 2002 and the subsequent NRL results.

SAMPLE	PRODUCT	LOT	QTY	Exp	Results
167877	Sterile Vials	n/a	~100	n/a	"In progress" as of 3/4/03
167876	Vial stoppers	n/a	Unkn.	n/a	"In progress" as of 3/4/03

MEETING WITH THE MABP: FEBRUARY 5, 2003 (Boston, MA)

A meeting was held to discuss the appropriate course of action for NECC. **Attachment #10** contains the minutes of this meeting.

VISIT TO FIRM: FEBRUARY 10, 2003 (Closeout and issuance of FDA-483)

On 2/5/03, [redacted] telephoned and left a voice mail for Mr. Cadden to inform him that there were violative sample results for subpotency and that the close out meeting would be held on 2/10/03. On 2/6/03, [redacted] received a voice mail from Mr. Cadden stating his intentions to investigate and institute a recall of betamethasone repository (lot 12102002@11).

The purpose of 2/10/03 closeout meeting included issuance of the FDA-483 (List of Observations), to request recall information for the methylprednisolone acetate recalled in 2002, to inform the firm of the complete results for samples obtained 12/18/03, and to find out the firm's intentions with respect to the violative lot within expiry and surrounding lots of similar products.

The closeout meeting took place at NECC on 2/10/03. In attendance from NECC were Barry J. Cadden, NECC Owner and Director of Pharmacy, [redacted] Educational Coordinator, was present in a secretarial role for NECC. In attendance from MABP [redacted] and [redacted] In attendance from the FDA NWE-DO were Investigators [redacted]

The visit began with a tour of the newly completed room that houses NECC's new Class 10 hood. The hood was certified by Scientific Air Analysis, Inc. (47 Fatina Dr, Ashland, MA 01701, [redacted]. The room contains the Class 10 hood, autoclave, incubator, sink, dishwasher, computer station and office area.

New England Compounding Center | FACTS #332851 | FEI# 3003623877
697 Waverly Street | KMJ/DAD | EI Start: 10/24/02
Framingham, MA 01702 | | EI End: 2/10/03

Mr. Cadden stated NECC had plans to work with a consultant, [redacted] of the Preble Group. See Exhibit #9 for the consultant information.

The following information was requested at the meeting:

1) For the recall of methylprednisolone acetate in 2002: distribution list (including addresses), reason for recall, recall strategy, time period of product distribution, total quantity distributed, total quantity returned in the recall, documentation of calls to clients, time period in which recall was conducted (start & stop), total quantity made and total put into vials, vial sizes and quantity of each that was made and product disposition.
2) For the pending recall of betamethasone repository (lot 12102002@11): all information above applicable to pre-recall period, copy of product labeling, recall initiation date, any complaints or adverse events reported and a recall contact.
3) Other Information: consultant CV, list of current stock on hand for all sterile injectable products, list of compounding that has taken place since 1/1/03 for all sterile injectable products and intentions with respect to similar products (ie., sterile injectable steroid suspensions).

[redacted] issued a new request for information from MABP dated 2/7/03. [redacted] provided a copy of the letter (Exhibit #10).

RECALL INFORMATION

On Friday, 12/13/02, the NWE-DO Recall Coordinator stated the district needed information from NECC to document and classify the recall of the methylprednisolone compounded product. I called Mr. Cadden that afternoon and discussed the need for recall information and to collect a larger quantity of vials for our sample (see below). He stated he would gather the information..

On Monday, 12/16/02, I called NECC to verify the receipt of the e-mail request for recall information and to answer any questions pertaining to the request. I left a message after I was told (by [redacted] that Mr. Cadden was "in the clean room". Lisa Cadden returned my call and informed me that Mr. Cadden did not receive my email on Friday. I explained that I sent it as a reply to an email from Mr. Cadden and that I would resend the email the following morning. I also verbally stated the list of requested information for the recall so the firm would have adequate notice. This information was not provided to NWE-DO until after 2/10/03. On 2/14/03, NWE-DO Recall Coordinator received two faxes from [redacted] containing the information for the NECC recall of betamethasone repository injection (6mg/ml, lot 12102002@11). On 2/18/03, NWE-DO Recall Coordinator received a fax from [redacted] containing the information for the NECC recall of methylprednisolone acetate (preservative-free, all lots compounded before 7/16/02). Please see Exhibit # 11 & 12 for these documents. On 2/21/03, the NWE-DO received additional information from [redacted] (via fax) informing the

FDA of NECC recall of further lots of betamethasone repository. This fax is attached as **Exhibit #13.**

CDER ASSIGNMENT & CPG 460.200 (PHARMACY COMPOUNDING)

The responses to the HFM-330 questions were obtained by inspectional visits and information provided by the MA State Board of Pharmacy (when followed by a *).

1) *Please determine from the Massachusetts Board of Pharmacy, whether NECC is operating in conformance with the applicable state law regulating the practice of pharmacy? Subsequent to the April 2002 joint FDA-State investigation, and referral to the Massachusetts Board of Pharmacy, what follow-up was done or what sanctions were taken by the Board?*

   There were no sanctions taken by the MABP against NECC following the April 2002 investigation. The Board is in the process of approving and adopting new regulations for pharmacy compounding firms. The MA applicable state laws reference the USP. Please see FDA-483 items for deficiencies observed at the firm.

2) *Does the NECC continue to fill patient specific prescriptions for each compounded product dispensed?*

   NECC dispenses and prepares products in bulk for administration to individualized patients pursuant to a receipt of a valid prescription from a prescriber. Bulk products produced in limited quantities at NECC are not compounded for third parties for resale. (*)

   Regarding patient specific information for filling non-sterile prescriptions: Mr. Cadden stated that NECC calls patients to ask them about their current medications for their computer patient profiles. He stated another reason to call the patient before making the compound is to verify the patient wants the compound since they are not usually covered under prescription insurance plans.

3) *What types and strengths of sterile products does the pharmacy compound? What quantities are being compounded? Is the pharmacy compounding copies of commercially available FDA-approved products (ie.,- products that have the same active ingredient, dosage form, and strength)? (typical batch size follows where known).*

   - Hyaluronidase 150u/ml- Discontinued by manufacturer (5,000 ml)
   - Triamcinolone Diacetate 40mg/ml- When unavailable (500 ml)
   - Methylprednisiolone Acetate PF 40mg/ml and 80mg/ml-
     Special order when unavailable (1,000 ml)

- Betamethasone Repository 6mg/ml and PF 6mg/ml- Special order when unavailable. (1,000 ml)

* Refer to Exh.#17 & 18 for other products compounded by NECC.

4) *Does NECC continue to assign unsubstantiated beyond-use dates? (designate expiration dates without basis)*

Mr. Cadden stated that beyond use dates are included on each formulation obtained from PCCA. Drug substances received, stored, or used at NECC are obtained only from FDA registered facilities. He stated he uses 6 month expiration dates for sterile products with preservative and 60 days for preservative-free.

It should be noted that samples obtained on 2/18/02 show that sample #169128 of methylprednisolone acetate preservative free (40 mg/ml x 1 ml, lot 11262002@5) had an expiration date of 1/10/03, which is approximately 45 days, not 60 days as stated by Mr. Cadden.

5) *Please obtain formulation information that will enable us to compare the compounded product formulations with the FDA-approved formulations. In certain circumstances, it may be appropriate for a pharmacist to compound a small quantity of a product that is only slightly different than a FDA-approved product that is commercially available (such as to remove a preservative or coloring agent for an individual patient with an allergy problem). In these circumstances, FDA will consider whether there is documentation of the medical need for the particular variation of the formulation for the particular patient. Does the pharmacy have documentation from the prescribers that demonstrates the medical need for the particular variation of the formulation for each individual patient?*

Please see Exhibit#14 for "Logged Formula Worksheets" utilized by NECC

6) *Does NECC compound drug products (including sterile products) in anticipation of receiving prescriptions? If so, what quantities are compounded on that basis? How do the amounts compare to the amount compounded after receiving valid prescriptions?*

Mr. Cadden stated *sterile products* are compounded *before* prescriptions are received. In general, approximately a 30 day supply would be maintained by NECC. The exception to this would be sterile products that can be filtered, such as ophthalmic products, which are compounded after receipt of a prescription. We did not have the opportunity to verify quantities compounded versus quantities dispensed on a monthly basis.

Mr. Cadden stated *non-sterile products* (creams, ointments, capsules, etc) are compounded *after* prescriptions are received.

7) *Does NECC use commercial scale manufacturing or testing equipment to compound drug products? What are the specific batch sizes that are prepared for each type of sterile product and how often is each batch prepared?*

In January 2003, NECC completed installation and certification of a "Class 10" Isolator biological hood. Mr. Cadden plans to begin utilizing this new area once he receives MABP approval. Refer to question 2 for typical batch sizes.

8) *Does NECC compound any products that have been removed or withdrawn from the market for safety reasons? If so, please obtain documentation.*

Mr. Cadden denies the firm compounds any products that have been removed or withdrawn from the market for safety reasons

9) *Has NECC instituted a formal written complaint system since the April 2002 FDA-State inspection?*

NECC does not have a formal written complaint system to date per Mr. Cadden. He stated complaints are still filed under specific facility or patient.

10) *Has NECC performed any corrective actions in response to the FDA 483 List of Observations issued at the conclusion of the April 2002 inspection?*

Mr. Cadden told us the only changes made were in response to the (b)(6), (b)(7)(C) adverse reactions and entailed the following: 1) expiration date was decreased from 6 months to 60 days for preservative free products, and 2) utilization of a contract facility (Eagle-Picher) to pre-sterilize vials for use in sterile products. See **Exhibit #5** for information from Eagle-Picher Industries, Inc. website (Miami, OK).

11) *Annually, how many prescriptions for compounded products does the NECC dispense?*

Mr. Cadden estimated NECC dispenses 20,000 prescriptions per year.

12) *Does NECC ship compounded products out of state? Was any of the lot of methylprednisolone acetate PF80mg/ml referenced in the MedWatch report shipped out of state?*

According to Mr. Cadden, NECC does ship compounded products out of state. The lot of methylprednisolone acetate PF referenced in the MedWatch was shipped out of state. On 2/5/03, [redacted] from MABP provided the states

NECC is licensed in as SC, FL, VA, ME, RI, NH, ID, NE, KS, VT, OH, MO, MT and CT (pending).

13) Does the NECC maintain a website concerning the products they compound?

Yes, the firm advertises services on the intranet at neccrx.com. The contents of the website, www.neccrx.com as of 10/11/02 are attached in Exhibit #15. Mr. Cadden states they do not accept online orders.

14) Please document the processes used to make the Methylprednisolone Acetate Preservative Free 80mg/ml product, including production scale, and any in-process controls.

See "Logged Formula Worksheet" provided by Mr. Cadden (Exhibit #16). This is the formula NECC obtained from PCCA to compound Methylprednisolone Acetate. Production scale varies according to what Mr. Cadden anticipates as need for the compounded product. There are no in-process controls per Mr. Cadden.

15) What quantity of compounded sterile products, including methylprednisolone acetate PF 80mg/ml are on hand for sampling?

We obtained samples of sterile injectable compounds on 12/12 & 18/02. Refer to Exhibit #17 for a list of current inventory as of 2/11/03.

OBJECTIONABLE CONDITIONS

Observation #1

For the preparation of sterile drug products distributed by your firm (such as those intended for injection), there is no adequate documentation available to verify they meet set standards (such as specifications and/or USP limits if applicable) or the shelf life (expiration dating period) of these products. This includes the absence of documentation to verify the following:

A. Personnel performing preparation steps are not contaminating the finished products.
B. Workspaces are cleaned and sanitized to prevent product contamination.
C. Equipment and supplies entering the product preparation area are decontaminated/cleaned to prevent product contamination.
D. The environment in the area where the filling and closing operations are performed is adequate to prevent product contamination (this includes the lack of documentation pertaining to environmental monitoring in the

New England Compounding Center
697 Waverly Street
Framingham, MA 01702

FACTS #332851
KMJ/DAD

FEI# 3003623877
EI Start: 10/24/02
EI End: 2/10/03

E. immediate area while product is exposed to the environment, such as during filling and prior to container closure).

F. All autoclave sterilization processes are suitable for the sterilization of drug product preparation equipment and components (which includes vial stoppers and bulk product). Some examples are:
   a. Lack of documentation to verify that all critical processing parameters being used are appropriate in ensuring that final products meet all standards (such as sterility). Critical processing parameters include sterilization time, temperature, size and nature of load, and chamber loading configuration.
   b. Records do not state the actual critical parameters used during processing.
   c. Lack of documentation to verify that the autoclave itself is maintained and calibrated to perform its intended function.
   d. The autoclave process used on bulk drug products does not have an effect on stability or product specifications.

F. The transfer of bulk drug product and equipment from the autoclave (after it went through an autoclave process) from one room to another room in which further preparation steps are performed in a laminar air flow workbench, is not introducing contamination into the finished product. All components, including drug substances, vials, and rubber stoppers, meet set standards making them suitable for their intended use.

G. Components and process water are not contaminating finished products.

H. Equipment used to measure the amount of ingredients/components are calibrated and maintained to perform their intended function.

I. Testing procedures and sampling procedures being performed for all drug products are representative of the lots/batches being tested.

J. That for each preparation of a sterile product or batch of sterile products there has been appropriate laboratory determination of conformity with purity, accuracy, sterility, and non-pyrogenicity, in accordance with established written specifications and policies.

K. Preparation steps are being performed in a correct manner since batch record preparation instructions are lacking significant preparation steps, which includes mixing procedures.

L. Final containers are capable of maintaining product integrity (i.e. identity, strength, quality, and purity) throughout the shelf life of the product.

M All drug products prepared and packaged at your site meet specifications and USP limits (if applicable) for the expiration dating period assigned. According to documentation and your statements, all drug products are assigned an expiration date of 60 days if they do not contain a preservative, three months if they are not filtered, and 6 months if they are filtered. No data was available for any of your products prepared at your firm to support these expiration date periods.

In addition, for all of the items above there were no written procedures available pertaining to the performance of these duties and processes.

Discussion of FDA 483 Observation 1

Mr. Cadden stated he did not have documentation of established standards or specifications for finished sterile products compounded by NECC. This included the verification that the above items (A thru M) have been addressed by NECC to ensure the quality of products compounded by NECC.

Mr. Cadden stated he was unable to provide data to support the assigned shelf life for finished sterile products compounded by NECC. Mr. Cadden stated that he utilized the recommendations on the product compounding formulas ("logged formula worksheets") received from PCCA. After learning of the the adverse reactions to methylprednisolone acetate in July 2002, Mr. Cadden stated he shortened the shelf life of preservative-free products from 6 months to 60 days. There was no product specific data available to support the use of either shelf life.

Mr. Cadden stated that he purchased Standard Operating Procedure (SOP's) from PCCA. After review of the SOP's, it was determined that they have not been revised for use at NECC. It was also noted that NECC does not follow the SOP's. Mr. Cadden stated he does not follow all of the SOP's. Refer to **Exhibit #8** for the NECC SOP's.

Observation #2

There are no written procedures pertaining to the handling of complaints, nor does your firm maintain a complaint file.

Discussion of FDA 483 Observation 2

Mr. Cadden stated that no formal complaint files are maintained by NECC. NECC has not established adequate written procedures for the handling of complaints and adverse events reported to the firm.

Observation #3

There was no documentation available for the handling and disposition of reports of patient problems, complaints, adverse drug reactions, drug product or device defects, and other adverse events reported. For example, after a medical facility reported adverse events associated with lot 05312002@16, your firm conducted a

recall of injectable steroid products and implemented shorter expiration dates and use of pre-sterilized vials. You stated you have no documentation available pertaining to an investigation being performed for this and other related lots which shows that adequate follow-up action was taken.

Discussion of FDA 483 Observation 3

Mr. Cadden stated he did not have documentation of an investigation or the subsequent changes made by NECC in response to the adverse events associated with methylprednisolone acetate lot 05312002@16. No written records were available to rationalize or confirm the implementation of shorter expiration dates and the use of pre-sterilized vials. There was also no written documentation to show follow up actions were being taken to ensure the effectiveness of corrective actions taken by the firm.

DISCUSSION WITH MANAGEMENT (2/10/03)

It was explained to Mr. Cadden that at this point the FDA is considering NECC a pharmacy compounder and not a drug manufacturer. Mr. Cadden stated he had retained the services of a pharmaceutical consultant. The consultant is supposed to meet with Mr. Cadden within the next week to determine a course of action.

[redacted] presented the FDA-483 to Mr. Cadden. Each item was reviewed with Mr. Cadden. Mr. Cadden was asked if he understood each point, to which he answered yes. Mr. Cadden was asked if he had any questions about each of the observation items, to which he answered no. [redacted] stated he was very familiar with the observations and would be able to assist Mr. Cadden in his written response.

Further details pertaining to this closing discussion is in this report under the heading entitled: "Visit to Firm: February 10, 2003". [redacted] stated they planned to have a written response to the FDA within two weeks. After the FDA-483 was issued and discussed, the inspection was concluded.

REFUSALS

Though information was not made readily available, there were no direct refusals from the firm.

ADDITIONAL INFORMATION

Guidance was received from HFM-330 throughout the entire investigation, including a teleconference on 12/16/02. During this teleconference, guidance was given regarding

samples to be collected and the composition and issuance of the FDA-483 (List of Observations).

On 1/23/03, NWE-DO received information that NECC had retained the services of [redacted] (Washington, DC) to represent him in regulatory matters. [redacted] requested available information through FOI. [redacted] discussed with the NWE-DO Compliance Branch that he would be representing NECC and Mr. Cadden; communication between the FDA and NECC from that point on (excluding the closeout on 2/10/03) occurred between [redacted] and NWE-DO Compliance Branch.

On 3/3/03 [redacted] of MABP related to Inv. Joyce that NECC had retained separate counsel to handle MABP related matters; however, he still retained [redacted] to handle FDA related matters.

At the time of this report, [redacted] stated MABP had not received a reply from NECC for their request for information dated 2/7/03. NECC requested and was granted an extension for submitting this information to MABP.

The list of current stock on hand for all sterile injectable products was received by fax on 2/11/03 (**Exhibit#17**). The list of compounding that has taken place since 1/1/03 for all sterile injectable products was received by email on 2/14/03 (**Exhibit #18**). [redacted] response to [redacted] questions on 2/10/03 regarding FDA regulations was received by NWE-DO on 2/21/03 and is attached as **Exhibit #19**.

The documents obtained from NECC to support the sample collections on 12/12 & 13/02 are attached as **Exhibit #20**.
Since the opportunity to observe production did not occur, no photographs were taken by the investigators.

ATTACHMENTS

FDA-482 Notice of Inspection (Dated 10/24/02)
FDA-482 Notice of Inspection (Dated 12/12/02)
FDA-482 Notice of Inspection (Dated 1/14/03)
FDA-482 Notice of Inspection (Dated 1/15/03)
FDA-482 Notice of Inspection (Dated 2/10/03)

1) CDER HFM-330 Assignment (Dated 8/2/02, 10 pages)
2) Collection Report for NYK Sample 193610 (4 pages)
3) FDA 463a Affadavit (Dated 12/12/02, 1 page)
4) FDA-484 Receipt for Samples (Dated 12/12/02, 2 pages)

5) Collection Reports for NWE Samples 12/12/02 (6 pages)
6) FDA 463a Affadavit (Dated 12/18/02, 1 pages)
7) FDA-484 Receipt for Samples (Dated 12/18/02, 2 pages)
8) Collection Reports for NWE Samples 12/18/02, 21 pages)
9) FDA Talk Paper (Dated 11/15/02, 2 pages)
10) Minutes of Meeting between MA State Board of Pharmacy and FDA NWE-DO (with attachments) (Dated 2/24/03, __pages)
11) FDA-483 Inspectional Observations (Dated 2/10/03, 3 pages)

EXHIBITS

1) Fax from (b) (6), (b) (7)(C) of (b) (6), (b) (7)(C) (Dated 11/1/02, 2 pages)
2) MABP Request for Information (10/02) and NECC response (Dated 11/18/02, 10 pages)
3) Email from NECC (dated 10/25/01, 1 page)
4) Analytical Research Laboratories Results for methylprednisolone lot 05312002@16 (4 pages)
5) Eagle-Picher Industries, Inc. background information (6 pages)
6) NECC sampling log to ARL (1 page)
7) NECC "Policies & Procedures for Compounding Sterile Products" (3 pages)
8) NECC SOP Manual (179 pages)
9) Curriculum Vitae of NECC Consultant (Fax Dated 2/11/03, 5 pages)
10) MA State Board of Pharmacy Request to NECC (Dated 2/7/03, 3 pages)
11) NECC Recall information (dated 2/14/03, 9 pages)
12) NECC Recall information (dated 2/18/03, 7 pages)
13) NECC Recall Information to NWE-DO Recall Coordinator (Dated 2/21/03, 7 pages)
14) Logged Formula Worksheets (21 pages)
15) NECC website information (Date accessed 10/11/02, 7 pages)
16) Methylprednisolone acetate "logged formula worksheet" (1 page)
17) NECC current inventory (dated 2/11/03, 2 pages)
18) NECC lots compounded since 1/1/03 (dated2/14/03, 2 pages)
19) NECC Response to 503A statement by [redacted] (Dated 2/21/03, 2 pages)
20) Supporting documents for sample collections (24 pages)

New England Compounding Center
697 Waverly Street
Framingham, MA 01702

FACTS #332851
KMJ/DAD

FEI# 3003623877
EI Start: 10/24/02
EI End: 2/10/03

[redacted]
NWE-DO

[redacted]
NWE-DO

CF

DEPARTMENT OF HEALTH & HUMAN SERVICES — Food and Drug Administration

NEW ENGLAND DISTRICT

MEMORANDUM

Date February 24, 2003

From [redacted] Consumer Safety Officer, NWE-DO / FDA
[redacted] Compliance Officer, NWE-DO / FDA

Subject February 5, 2003 Meeting with Massachusetts Board of Pharmacy / Division of Professional Licensure (239 Causeway Street, Boston, MA 02114).

To Central File

Firm: New England Compounding Center
697 Waverly Street
Framingham, MA
FEI: 3003 623 877

Background

This meeting was arranged at the request of [redacted], NWE-DO Compliance Officer, via email to Charles Young, Executive Director, on January 30, 2003. The meeting was held to review the inspectional history of the New England Compounding Center and develop a joint strategy for achieving safe compounding practices at the firm.

In attendance at the meeting were:

Representing the New England District—

Gail Costello, District Director
David Elder, Compliance Branch Director
[redacted], Compliance Officer
[redacted], Supervisory Consumer Safety Officer
[redacted], Consumer Safety Officer

Representing the Office of Compliance, CDER (via teleconference)—

[redacted], OC / DNDLC
Kathleen Anderson, OC / DNDLC
[redacted], ORO / DFSR

Representing the Commonwealth of Massachusetts—

Jean Pontikas, Director, Division of Professional Licensure
Charles Young, Executive Director, Board of Pharmacy
James Coffey, Associate Director, Board of Pharmacy
[redacted], Supervisory Investigator, Board of Pharmacy
[redacted], Investigator, Board of Pharmacy
Susan Manning, Legal Counsel, Board of Pharmacy

Note: This memorandum has been prepared in accordance with Staff Manual Guide FDA 2126.2

Summary of Meeting

Mr. Young and [redacted] facilitated introductions.

[redacted] began with an overview of the inspectional history of New England Compounding Center (NECC). This included a brief description of the recent regulatory history of Pharmacy Compounding.[1]

[redacted] then presented a table summarizing the results of FDA's current sample analyses.[2] [redacted] discussed current investigational findings.[3] It was stated that the FDA's next step would be to notify the firm of the violative sample results and inquire of his intentions regarding the violative product still in commerce. It was anticipated that the firm would initiate a voluntarily recall of the violative product.[4] If NECC does not take action regarding the violative lot, then depending on the quantities of the lot available FDA may initiate a seizure of the product. A Form FDA–483 (List of Inspectional Observations) will be issued to NECC with state representatives present at the FDA closeout meeting with NECC. [redacted] and Kathleen Anderson reminded everyone that in a similar situation with a South Carolina compounding pharmacy, FDA issued a press release when the firm failed to take recall action in a timely manner.

A discussion was held to decide if NECC should be considered a manufacturer or a compounder. It was decided that current findings supported a compounding role. The FDA discussed their ability to take action (through seizure) against the adulterated lot of Betamethasone that is still within expiry. The issues of NECC's poor compounding practices would not necessarily be ultimately resolved by such an action. It was decided that the state would be in a better position to gain compliance or take regulatory action against NECC as necessary. The state favored recall of the violative product

[1] See Attachment 1.
[2] See Attachment 2.
[3] See Form FDA–483 (Inspectional Observations), Attachment 3.
[4] The firm has committed to recall this product.

within expiry. The state does not have the authority to subpoena records without cause or to embargo product, but agencies within their umbrella may be able to provide assistance in those matters. The state would ask Mr. Cadden, owner of NECC, to appear before the Board of Pharmacy to answer to the current complaints.

[redacted] stated that NECC is licensed as a pharmacy provider in the following states—South Carolina, Florida, Virginia, Missouri, Maine, Rhode Island, New Hampshire, Nebraska, Idaho, and Montana. NECC is pursuing licensure in Connecticut, Ohio, Vermont, and Kansas.

Susan Manning stated Massachusetts pharmacy law states that pharmacists must act in accordance with USP recommendations. She stated this alone would imply he could be held to those standards by the state. She requested of the FDA a list of the current inspectional observations and where NECC differs from acceptable practice per USP standards. It was decided that Ms. Anderson would work on documenting the deviations from USP standards for the state. Ms. Manning stated although the state's authority does not include the ability to fine pharmacists, the state is able to take actions against a pharmacy's license, including revocation and suspension.

The state's pharmacy compounding regulations that are under review are a blend of USP standards and regulations from three other states that already have such regulations in place (including Georgia and South Carolina).

The state requested the following information[5] from the FDA:

- Examples of previous Consent Agreements
- MedWatch reports regarding Adverse Events from products compounded by NECC.
- A list of NECC deviations from acceptable practice (referring to FDA's inspectional findings)
- Previous and current FDA 483 (List of Observations) issued to NECC, with available documentation to support the findings.
- Copies of FDA EIRs for NECC (April 2002 and current inspection when available)
- Analytical Worksheets for sample collection and analysis.
- Copy of regulatory action taken by the FDA against Professional Compounding Centers of America (PCCA).

Summary

Mr. Elder concluded the meeting by summarizing the discussions and emphasizing the potential for serious public health consequences if NECC's compounding practices, in particular those relating to sterile products, are not improved. The point was made that, so long as a pharmacy's operations fall within the scope of the practice of pharmacy (as

[5] This information was forwarded to the Board of Pharmacy (to the attention of Ms. Manning) via Federal Express on February 11, 2003.

outlined in FDA's Compliance Policy Guide 460.200), FDA will generally continue to defer to state authorities for regulatory oversight. In such cases FDA will seek to engage cooperative efforts aimed at achieving regulatory compliance and ensuring the safety and quality of compounded products.

[redacted]
Consumer Safety Officer
New England District, FDA

[redacted]
Compliance Officer
New England District, FDA

Attachments (3)

Distribution Page—February 5, 2003 Meeting with Massachusetts Board of Pharmacy

bcc:

[redacted]

Central File
Reading File
Legal Reading File

[redacted](HFD–310)
Anderson (HFD–310)

U:[redacted]/ Inspections / NECC / Meeting with State / Memorandum of Meeting.doc

ATTACHMENT 1

INSPECTIONAL HISTORY OF NEW ENGLAND COMPOUNDING CENTER (NECC)

Presentation to Board of Registration in Pharmacy, Division of Health Professions Licensure, Department of Public Health, Commonwealth of Massachusetts

February 5, 2003

April 2002

- New England District receives inspection assignment from CDER / Office of Compliance / DPDSC. Two MedWatch reports implicated product compounded at NECC in adverse events (dizziness, shortness of breath, diaphoresis, drop in blood pressure to 55/44).
- Product in question is Betamethasone Repository 6 mg/ml (Betamethasone Acetate 3mg/ml / Betamethasone Sodium Phosphate 3 mg/ml USP), available commercially as Celestone Soluspan.

April 2002

- This is the same formulation that was involved in 13 hospitalizations (including 5 cases of meningitis, 3 of which were fatal) and was compounded at Doc's Pharmacy in Walnut Creek, CA.
  - As a result of this incident the Atty General of California brought a formal accusation (on behalf of the Exec. Officer of the Board of Pharmacy) before a judge.

April 2002

- FDA team, along with Leslie Doyle of BRP conducted an inspection of NECC.
- FDA issues list of observations (Form 483).
- BRP pursues independent follow-up

July 2002 (and ongoing)

- Second inspection assignment is received from CDER as a result of 2 additional MedWatch reports associated with ***another*** product from NECC, in this case Methylprednisolone Acetate Suspension (Injectable, Preservative Free), 80 mg/ml.

- Both patients were hospitalized (pain, headache) and recovered. Units from suspect lot were collected from a (b) (6), (b) (7)(C) hospital.

220

July 2002 (and ongoing)

- Assistance of BRP requested as before.
- Section 503A of FDCA has since been invalidated by U.S. Supreme Court
- Inspection is initiated in August. Multiple samples are collected.

July 2002 (and ongoing)

- ***Urgent Care, Spartanburg, SC.***
  - On September 16, 2002 there is a recall of Methylprednisolone Acetate Injection compounded by this pharmacy as a result of fungal meningitis (4 patients contract this infection, 1 dies).
  - Nationwide alert issued by FDA on November 15, 2002 for all injectable products produced by Urgent Care.
  - Cease and desist order is issued by SC Board of Pharmacy.

July 2002 (and ongoing)

- ***Urgent Care, Spartanburg, SC.***
  - MMWR (CDC, December 13, 2002) publishes assessement of this incident (*Exophiala* Infection from Contaminated Injectable Steroids Prepared by a Compounding Pharmacy — United States, July–November 2002).

January 2003

- Samples with significant findings
  - 193610 *Burkholderia cepacia* and *Sphingomonas paucimobilis* (Methylprednisolone Acetate Injection)
  - 169127 Subpotency (Betamethasone Repository) Expired on Jan 29, 2003
  - 169129 Subpotency (Betamethasone Repository) **Expires on June 8,2003.** ***This product is adulterated under Sec. 501(b) of FDCA.***
  - 169128 Superpotency (Methylprednisolone Acetate Injection) Expired on Jan 10, 2003

224

Existing Concerns

- Analytical evidence demonstrates inability of NECC to reliably compound suspensions with dose uniformity.

- Sterilization techniques and aseptic practices continue to raise questions, despite no positive (nonsterile) results from latest samples. Absence of evidence is not evidence of absence.

ATTACHMENT 2

SUMMARY OF SAMPLE COLLECTION/ANALYSIS FOR NECC
FEBRUARY 5, 2003

SAMPLE	PRODUCT	LOT	QTY	Exp	Results
169126	Methylprednisolone AC (PF) 80 mg/ml x 1 ml	11262002@4	20	1/25/03	Assay= Within Range
169127	Betamethasone Repository (PF) 6mg/ml x 5ml (BSP+BA)	11302002@1	10	1/29/03	Assay= Subpotent BSP 77.4 (O); 74.6 (C/A) BA 71.6 (O); 71.0 (C/A)
169128	Methylprednisolone AC (PF) 40 mg/ml x 1 ml	11262002@5	50	1/10/03	Sterility= Negative Endotoxin- "not performed" Assay= Superpotent 131.4 (O) & 133.1% (C/A)
169129	Betamethasone Repository 6mg/ml x 2 ml	12102002@1 1	50	6/8/03	Sterility= Negative Endotoxin= Negative Assay- subpotent BSP 67.0 (O); 62.0 (C/A) BA 59.8 (O); 58.7 (C/A)
169130	Methylprednisolone AC (PF) 80 mg/ml x 1 ml	11262002@4	50	1/25/03	Sterility= Negative Endotoxin= Negative
169131	Triamcinolone Acetonide 40 mg/ml x 5 ml	112020002@ 8	34	2/18/03	Sterility= Negative Endotoxin "not performed"
169132	Prochlorperazine Edisylate 5 mg/ml x 10 ml	11112002@1 1	18	2/9/03	Sterility= Negative Endotoxin "not performed"
169133	Saline PF 10% injectable x 15 ml	12122002@1 4	5	3/12/03	Sterility= Negative Endotoxin= "not performed"
208553	Betamethasone Repository (PF) 6mg/ml x 2ml	11302002@1	50	1/29/03	Sterility= Negative Endotoxin= "not performed"
	Sterile Vials				
	Vial stoppers				

1. PF= Preservative Free (for some products, NECC makes product both with and without preservative)
2. Betamethasone Repository= Betamethasone Sodium Phosphate & Betamethasone Acetate.

SAMPLE	PRODUCT	LOT	QTY	Exp	Results
193610 (9/13/02)	Methylprednisolone AC (PF) 80MG/ML INJ		16		1/14= *Sphingomonas paucimonas* 4/14= *Burkholderia cepacia*

SUMMARY OF FDA INSPECTIONAL OBSERVATIONS FOR NECC
FEBRUARY 5, 2003

ASSAY ISSUES

1) No documentation to verify sterile drug products meet set standards, such as:
    a. No specifications (ie. USP or other) are set for finished products
    b. No evidence products meet assigned shelf life.

2) Preparation: No documentation of the following:
    a. Equipment used to measure components are calibrated and maintained to perform their intended function
    b. Preparation steps are being performed in a correct manner since batch record preparation instruction sare lacking significant preparation steps, including mixing and transfilling procedures.
    c. All components (drug substances, water, vials, rubber stoppers) meet set standards making them suitable for their intended use and don't contaminate the finished product.
    d. Testing and sampling procedures performed for finished drug products are representative of the lots/batches being tested.

3) Testing/Sampling: No documentation of the following
    a. No testing is done to confirm product meets specifications. (the only finished product testing for selected lots is sterility and endotoxin).
    b. Testing and sampling procedures performed for finished drug products are representative of the lots/batches being tested.

STERILITY ISSUES

1) Lack of assurance/documentation:
    a. Equipment, supplies and workspaces are sufficiently cleaned to prevent contamination of finished product.
    b. No Environmental Monitoring of Clean Room.
    c. All autoclave sterilization processes are suitable for the sterilization of drug product preparation equipment and components.
    d. Transfer of bulk drug product and equipment from the autoclave (from one room thru ante-room to "clean room") for further processing doesn't contaminate product.
    e. Transfilling procedures are being performed in a correct manner since batch record preparation instructions lack transfilling instructions.

ATTACHMENT 3

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT OFFICE ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
One Montvale Avenue, 4th Floor Stoneham, MA 02180 [redacted]	10/24, 12/12&18/02, 1/14-15/03, 2/10/03
	FEI NUMBER 3003623877

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: Barry J. Cadden, Director of Pharmacy

FIRM NAME	STREET ADDRESS
New England Compounding Center	697 Waverly Street
CITY, STATE AND ZIP CODE Framingham, MA 01702	TYPE OF ESTABLISHMENT INSPECTED Pharmacy

DURING AN INSPECTION OF YOUR FIRM WE OBSERVED:

The below observations pertain to drug products that personnel prepare at your firm for which you claim are sterile (for example, injections) and are prepared in anticipation of a prescription.

1. For the preparation of sterile drug products distributed by your firm (such as those intended for injection), there is no adequate documentation available to verify they meet set standards (such as specifications and/or USP limits if applicable) or the shelf life (expiration dating period) of these products. This includes the absence of documentation to verify the following:
   A. Personnel performing preparation steps are not contaminating the finished products.
   B. Workspaces are cleaned and sanitized to prevent product contamination.
   C. Equipment and supplies entering the product preparation area are decontaminated/cleaned to prevent product contamination.
   D. The environment in the area where the filling and closing operations are performed is adequate to prevent product contamination (this includes the lack of documentation pertaining to environmental monitoring in the immediate area while product is exposed to the environment, such as during filling and prior to container closure).
   E. All autoclave sterilization processes are suitable for the sterilization of drug product preparation equipment and components (which includes vial stoppers and bulk product). Some examples are:
      a. Lack of documentation to verify that all critical processing parameters being used are appropriate in ensuring that final products meet all standards (such as sterility). Critical processing parameters include sterilization time, temperature, size and nature of load, and chamber loading configuration.
      b. Records do not state the actual critical parameters used during processing.
      c. Lack of documentation to verify that the autoclave itself is maintained and calibrated to perform its intended function.
      d. The autoclave process used on bulk drug products does not have an effect on stability or product specifications.

   F. The transfer of bulk drug product and equipment from the autoclave (after it went through an autoclave process) from one room to another room in which further preparation steps are performed in a laminar air flow workbench, is not introducing contamination into the finished product. All components, including drug substances, vials, and rubber stoppers, meet set standards making them suitable for their intended use.
   G. Components and process water are not contaminating finished products.
   H. Equipment used to measure the amount of ingredients/components are calibrated and maintained to perform their intended function.
   I. Testing procedures and sampling procedures being performed for all drug products are representative of the lots/ batches being tested.
   J. That for each preparation of a sterile product or batch of sterile products there has been appropriate laboratory

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (Print or Type)	DATE ISSUED

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT OFFICE ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
One Montvale Avenue, 4th Floor Stoneham, MA 02180 [redacted]	10/24, 12/12&18/02, 1/14-15/03, 2/10/03
	FEI NUMBER 3003623877

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: Barry J. Cadden, Director of Pharmacy

FIRM NAME	STREET ADDRESS
New England Compounding Center	697 Waverly Street
CITY, STATE AND ZIP CODE Framingham, MA 01702	TYPE OF ESTABLISHMENT INSPECTED Pharmacy

determination of conformity with purity, accuracy, sterility, and non-pyrogenicity, in accordance with established written specifications and policies.

K. Preparation steps are being performed in a correct manner since batch record preparation instructions are lacking significant preparation steps, which includes mixing procedures.

L. Final containers are capable of maintaining product integrity (i.e. identity, strength, quality, and purity) throughout the shelf life of the product.

M. All drug products prepared and packaged at your site meet specifications and USP limits (if applicable) for the expiration dating period assigned. According to documentation and your statements, all drug products are assigned an expiration date of 60 days if they do not contain a preservative, three months if they are not filtered, and 6 months if they are filtered. No data was available for any of your products prepared at your firm to support these expiration date periods.

In addition, for all of the items above there were no written procedures available pertaining to the performance of these duties and processes.

2. There are no written procedures pertaining to the handling of complaints, nor does your firm maintain a complaint file.

3. There was no documentation available for the handling and disposition of reports of patient problems, complaints, adverse drug reactions, drug product or device defects, and other adverse events reported. For example, after a medical facility reported adverse events associated with lot 053 12002@16, your firm conducted a recall of injectable steroid products and implemented shorter expiration dates and use of pre-sterilized vials. You stated you have no documentation available pertaining to an investigation being performed for this and other related lots which shows that adequate follow-up action was taken.

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (Print or Type)	DATE ISSUED

The Commonwealth of Massachusetts
Executive Office of Health and Human Services
Department of Public Health
250 Washington Street, Boston, MA 02108-4619

Board of Registration In Pharmacy
239 Causeway Street, 5th Floor
Boston, MA 02114

MITT ROMNEY
GOVERNOR

KERRY HEALEY
LIEUTENANT GOVERNOR

RONALD PRESTON
SECRETARY

CHRISTINE C. FERGUSON
COMMISSIONER

October 04, 2004

Barry J. Cadden, R.Ph.
Manager of Record
New England Compounding Center
697 Waverly Street
Framingham, MA 01702

RE: Docket Number DS-03-055/ PH-03-066/ New England Compounding Center (Lic. No. 2848) and Barry Cadden, R.Ph., License No. 21239

Dear Mr. Cadden:

The Board has voted to resolve the above-referenced case by offering you a consent agreement to resolve issues related to the above-referenced matter.

Please be advised that if you choose not to enter into the Agreement, the Board will proceed to a formal hearing, pursuant to G.L. c. 30A.

Please return both copies of the Agreement to the Board at your earliest convenience but no later than within ten (10) days of their receipt. The Board will then sign them and an executed copy will be returned to you.

Please contact Associate Director James D. Coffey at 617-727-6095 if you have any questions regarding this matter.

Sincerely,

Charles R. Young, R.Ph.
Executive Director
Board of Registration In Pharmacy

Enc.
By Certified Mail 7003 1010 0003 3509 7959

COMMONWEALTH OF MASSACHUSETTS

SUFFOLK COUNTY

BOARD OF REGISTRATION
IN PHARMACY

In the Matter of
NEW ENGLAND
COMPOUNDING CENTER
Registration No. 2848
BARRY J. CADDEN, R.Ph.
License No. 21239

DOCKET NOS. DS-03-055
PH-03-066

CONSENT AGREEMENT

The Board of Registration in Pharmacy ("Board") and NEW ENGLAND COMPOUNDING CENTER (Pharmacy Registration No. 2848), located at 697 Waverly Road, in Framingham, Massachusetts ("Registrant"), and BARRY J. CADDEN, R.Ph. ("Licensee") Pharmacist License No. 21239 and Manager of Record of Registrant, do hereby stipulate and agree that the following information shall be entered into and become a permanent part of the file of Registrant which is maintained by the Board:

1. The parties enter into this Consent Agreement ("Agreement") to resolve disputed matters arising out of the complaints pending against Registrant and Licensee, respectively, as Docket Nos. DS-03-055 and PH-03-066 ("Complaints").

2. The Registrant agrees that this Agreement has been entered into as a result of an adverse event complaint report investigated by the U.S. Food and Drug Administration alleging that Registrant, while the Licensee was Manager of Record, failed to comply with accepted standards in compounding a certain order for methyprednisolone acetate preservative free 80mg/ml suspension

3. Accordingly, the Registrant agrees to the following:

   a. The conduct described in Paragraph 2. above constitutes professional misconduct warranting disciplinary action by the Board pursuant to G.L. c. 112, § 61 and 247

CMR 9.01(1);

b. The Registrant and Licensee are hereby REPRIMANDED by the Board and the Registrant's pharmacy registration and Licensee's pharmacist license are hereby placed on probation for a minimum three (3) year period (the "Probationary Period"), commencing on the date this Consent Agreement is executed by the Board; and

c. The Registrant and Licensee agrees that during the Probationary Period:

1) Registrant's manager of record shall be required to develop and implement written policies and procedures to provide for and insure that USP Guidelines are followed and the Registrant performs in accordence with USP Guidelines and 247 CMR;
2) Registrant's manager of record shall be required to update standard operating procedures on a quarterly basis
3) Registrant may be inspected by the Board;
4) Registrant will keep a written report of each adverse event reported and make such reports available for review by the Board upon request during inspections;
5) Registrant will provide an after business hours telephone number for consumer use and have written protocols for after business services; and

4. Registrant and Licensee acknowledge that the Registrant and Licensee must apply in writing to the Board for termination of the Probationary Period and that termination of the Probationary Period shall be granted only if all of the conditions set forth above in Paragraph 3.c. have been met. The Board may request a conference to discuss the merits of such request

5. This Agreement and its contents shall be incorporated into the records maintained by the Board. This Agreement and is contents are matters of public record, and are subject to disclosure without limitation to the public and equivalent state licensing boards.

7. The Board agrees that in return for the execution and fulfillment of the requirements of this Agreement by the Registrant and Licensee, the Board will not advance the prosecution of the Registrant and Licensee pursuant to the Complaint; any and all other rights of the Board to take action within the scope of its authority are expressly reserved.

8. The Registrant and Licensee understand and agree that the failure to accept the terms of this Agreement shall nullify the representations contained herein, and permit the Board to initiate formal adjudicatory action under the State Administrative Procedure Act, G.L. c. 30A, and the Standard Adjudicatory Rules of Practice and Procedure, 801 CMR 1.00 *et. seq.*

9. The Registrant and Licensee understand and agree that the decision to enter into this Agreement and to accept the terms and conditions herein described is a final act and is not subject to reconsideration or judicial review.

10. The Registrant and Licensee state legal counsel has been consulted in connection with the decision to enter into this Agreement and if not, that there was an opportunity to do so.

11. The Registrant and Licensee certify this document entitled "Consent Agreement" has been read. The Registrant and Licensee understand that, by executing this Agreement, the Registrant and Licensee are waiving any right to a formal hearing with rights to confront and cross-examine witnesses, to call witnesses, to present evidence, to testify on its own behalf, to contest the allegations, to present oral argument, to appeal to court in the event of an adverse ruling, and all other rights set forth in G.L. c. 30A and 801 CMR 1.01 *et seq.*

NEW ENGLAND
COMPOUNDING CENTER

By:_____
Barry J. Cadden, R.Ph.
Director of Pharmacy

Date:_____

_____
Barry J. Cadden, R.Ph.
Manager of Record
Date:_____

BOARD OF REGISTRATION
IN PHARMACY

By:_____
James T. DeVita, R.Ph.
President

Effective Date:_____

Board Dec. No.
Cert Mail No. 7003 1010 0003 3509 7959

[redacted]

[redacted]

[redacted]

November 11, 2004

Susan Manning, Esq.
The Commonwealth of Massachusetts
Board of Registration in Pharmacy
239 Causeway Street
Boston, MA 02114

Re: Docket Number DS-03-055/PH-03-066/New England Compounding Center (Lic. No. 2848) and Barry Cadden, R.Ph. License No. 21239

Dear Ms. Manning:

On behalf of my clients, Barry Cadden, R.Ph., and New England Compounding Center ("NECC"), I am writing to respond to Mr. Young's October 4, 2004 letter regarding the above-referenced matters. Thank you for the courtesy of extending the time for this reply.

As you may be aware, NECC is now licensed in 44 states, and has applications pending in 2 others.[1] That resume speaks volumes to the quality of its products, and to its reputation. More significantly, its success in passing the due diligence inquires and inspections that are attendant to those licenses is a testament to both NECC's and Mr. Cadden's commitment to quality assurance and regulatory compliance. Indeed, since contracting with a national expert in Aseptic Compounding ([redacted] in 2002, NECC has implemented policies and procedures that address – and in some instances exceed – the proposed probationary conditions in paragraph 3.c. of Mr. Young's letter. With Mr. Brennan's guidance, NECC already has:

- Conducted an independent review and evaluation of its sterile compounding practices

[1] NECC currently does business in 4 states that do not require a license/permit Georgia, New Jersey, Pennsylvania, Wisconsin, and plans to apply for licensure in the two remaining states Tennessee and Arkansas.

- Developed a comprehensive set of sterile products compounding standard operating procedures
- Implemented a comprehensive quality management program that includes:
  - Sterile products specifications.
  - Staff, facilities, and process controls.
  - Aseptic process validation.
  - Ongoing environmental bioburden monitoring.
  - Batch quality control release testing that includes pH, absence of visible foreign particulates, closure integrity, sterility and endotoxin.
  - Frequent monitoring of drug content potency.
- Implemented a formal complaint management/corrective and preventive action (CAPA) program.
- Established USP <797> gap-analysis and standards.

In addition, NECC has recently formalized a "Quality Assurance Team" which includes the director of pharmacy, the head technician, a sterile technician, the general manager and the marketing manager. The Team meets monthly with the stated mission of eliminating pharmacy error. Finally, following the suggestion in Mr. Young's letter (at paragraph 3.c.5), NECC has formalized an after business hours protocol to insure 24/7 consumer access. NECC's commitment to all these initiatives should be well known to the Board, which has inspected the facility three times since last February (twice, with a representative from the FDA):

- February 20, 2004 — MA Board of Registration in Pharmacy [redacted]
- September 23, 2004 — MA Board of Registration in Pharmacy [redacted] and FDA – [redacted]
- September 28, 2004 — MA Board of Registration in Pharmacy [redacted] and FDA – [redacted]

All of these inspections have been without incident.

While I think it fair to say that the product of NECC's interaction with the Board – as demonstrated above – is a success story, such would not be the case if the resolution were to include a disciplinary sanction (including the reprimand proposed in Mr. Young's

letter). The collateral consequences to many, if not all of NECC's 42 other licenses, would be potentially fatal to the business.[2] Such a catastrophe is clearly not the intended result of the Board's proposed reprimand, nor is it warranted in this case. The Board's mandate is to protect the public health safety and welfare, not to punish its licensees (see, e.g., Gurry v. Board of Public Accounting 394 Mass. 118, 127-128 (1985); Levy v. Board of Registration in Medicine 378 Mass. 519, 527 (1979).

Mr. Cadden and NECC have demonstrated their commitment to remediation, and are prepared to continue to do so. In that regard, NECC and Mr. Cadden will agree to all of the probationary terms offered in Mr. Young's letter, and will further agree to bear the burden and cost of monitoring and reporting their compliance.[3] That result could be accomplished through a non-disciplinary resolution such as a continuance (pending a period of monitoring) or a "stayed probation." Whatever the vehicle, Mr. Cadden and NECC are ready, willing and able to insure all of the public protection components of Mr. Young's proposed resolution, but respectfully request that the Board do so without also imposing discipline which may destroy their business.

Both Mr. Cadden and I are available to meet with you, Mr. Young and/or the Board itself to discuss resolution of this matter. We look forward to your reply.

Very truly yours,

[redacted]

PC/mjc

[2] Once disclosed, the reprimand will surely result in inquiries/investigations in those other jurisdictions. Regardless of the derivative actions taken, the attendant legal and administrative costs will be devastating.

[3] NECC is prepared to extend [redacted] contract to provide ongoing monitoring – on such matters as the Board may prescribe – with regularly scheduled written reports to the Board.

DEPARTMENT OF HEALTH & HUMAN SERVICES — Food and Drug Administration

NEW ENGLAND DISTRICT

MEMORANDUM

Date January 26, 2005

From [redacted]
NWE-DO

Subject Inspection/Investigation of
New England Compounding Center
697 Waverly Street
Framingham, MA 01702

To Kathleen Anderson, Acting Team Leader
Compounding Team, HFD-316
Division of New Drugs & Labeling Compliance

Thru [redacted]
NWE-DO

An investigation/limited inspection of this Compounding Pharmacy was conducted jointly with the Massachusetts Board of Pharmacy (MABP) per request of CDER, Division of New Drugs & Labeling Compliance, Compounding Team, HFD-316 (FACTS 536354). This investigation was mainly to obtain information about the firm's compounding practices, as they relate to the compounding of Trypan blue products.

I was accompanied on this investigation/limited inspection of the New England Compounding Center (NECC) by [redacted] Investigator & [redacted] Quality Assurance Coordinator, who are both from the MABP.

On September 23, 2004 our credentials were shown & FDA 482, Notice of Inspection, was issued to Mr. Barry Cadden, Director of Pharmacy & Owner of the New England Compounding Center (NECC). Mr. Cadden acknowledged that he is the most responsible person in the firm. I was introduced to Mr. Gregory A. Conigliaro, General Manager & Co-Owner of NECC. Mr. Conigliaro reported that he just joined the company about eight months ago & that he is a Civil Engineer by profession. He provided the following information. The corporate structure of NECC is as follows:

President	-	Carla Conigliaro
Vice President	-	Barry Cadden
Treasurer	-	Greg Conigliaro
Clerk	-	[redacted]

I asked Mr. Cadden if the corrective actions that were promised by him on the last EI of 2/10/03 were already implemented. Last EI of 2/10/03 was classified "OAI" with referral to Massachusetts State Board of Pharmacy. FDA 483, Inspectional Observations, was issued for: (1) inadequate documentation to verify sterile drug products dispensed meet set of standards, such as specifications or assigned shelf life; (2) no SOPS for handling complaints and failure to maintain complaint files; and (3) lack of documentation for a specific reported adverse event.

Inspection of firm's new set of procedures & related documents showed that corrective actions have been implemented.

I asked Mr. Cadden if he is compounding & dispensing Trypan Blue. He said he does. I asked him if he has anything in stock. He said no, because he just compounds the drug if he receives the prescriptions for certain patients. While showing us the "Clean Room" where compounding takes place, we had to pass through a small laboratory where some tests were being performed. I noticed a drawer that was identified as "Trypan Blue". I requested him to open the drawer. There were 189-1ml vials of Trypan Blue PF 0.1% Injectable, Lot #07272004. See labeling shown as Exhibit #1. I told Mr. Cadden that Trypan Blue is not an FDA approved product & as such he should not be compounding & dispensing it. Mr. Cadden stated that he did not know that it is not an approved product. He told one of the employees in the laboratory to put the vials in quarantine which he told us will be eventually destroyed.

I told Mr. Cadden that I have to obtain some information from him as part of my assignment.

I gave Mr. Conigliaro a list of some of the questions in the assignment (#3, 4, 5, 7, 10, 11, 12, 15, 16 & 17). I did not list down the other questions in the assignment because I thought that it would be better if I ask him the questions directly.

Mr. Cadden stated that he will have to talk with his lawyer if it is okay to supply the information/answer the questions I had given him. He also stated that his lawyer is on vacation & would not be back until 9/27/04. The lawyer's name is [redacted] from Newton, MA.

[redacted] went back to the firm on 9/28/04 & met with Mr. Cadden & Mr. Conigliaro.

I asked Mr. Conigliaro if he was able to answer the questions I had listed down on our last visit. He stated that he has made some responses to the questions/information I had requested, in draft form & that he has to show their lawyer for approval before he could give it to me.

I requested Mr. Cadden for Trypan Blue labels which he provided (see Exhibit #2). A copy of the Certificate of Analysis for Trypan Blue (Exhibit #3) that came with the shipment of the Trypan Blue raw material that was in stock, Lot #C107217, was obtained. The supplier was PCCA, Houston, Texas.

The following information was obtained from Mr. Cadden when I questioned him about the one hundred eight nine (189) vials of Trypan Blue that I found in one of the drawers in the laboratory that was labeled "TYRPAN BLUE" on 9/23/04.

- He did not have to put the Trypan Blue vials in quarantine, which would eventually be destroyed as he told me on 9/23/04, after they had spoken to their lawyer.

- Their lawyer had told them that there is no regulation which states that Compounding Pharmacies cannot compound FDA non-approved drugs.

- That he dispensed Trypan Blue on 9/24, 25, 26, 27 & 28/04 as shown in log (Exhibit #4).

- That he intends to compound & dispense Trypan Blue until FDA/MABP will put in writing that they cannot compound it & dispense it and the reason why.

When I started asking Mr. Conigliaro the rest of the questions in the assignment, he became indignant & he said that he does not really have the time to sit with us & answer all those questions. He said if I could give him the list of questions, he would prepare the answers & give everything to me in one piece, after he shows it to their lawyer.

Mr. Cadden also told Mr. Conigliaro, "Don't answer anymore questions!"

Mr. Conigliaro questioned how Trypan Blue came into the picture. I told him it is part of my assignment from headquarters. Then he wanted to know specifically who issued the assignment & I gave him Kathy Anderson's name. He also started questioning FDA's jurisdiction on Compounding Pharmacies.

I told Mr. Conigliaro that FDA received a complaint re: Trypan Blue, so we have to do our investigation, because FDA has to respond to the complaint & we have to notify MABP also.

Mr. Conigliaro asked me who the complainant was & I told him I don't know. He said it's probably one of their competitors. He also said that he was sorry if he sounded mean. He explained that he had to leave early, had a lot of things to finish & just did not have the time to sit with us to answer our questions.

I wrote down the remaining list of questions in the assignment & left them with Mr. Conigliaro.

On October 1, 2004, I received a 22-page fax document from Mr. Conigliaro, which constituted his responses to the written questions I had given him. This was followed by a hardcopy (Exhibit #5) which I received on October 5, 2004. I showed these responses to [redacted]Ann Simoneau, CO, NWE-DO to update them about the status of the assignment & told them about the firm's attitude.

I requested [redacted] for a copy of a written report of what sanctions were taken by the MABP as follow-up from the EI of 2/03. [redacted] stated that the cases are still pending Board & as such are not releasable at that time. The assignment in regards to Trypan Blue is also pending Board & when they become releasable, he will forward them to me.

I told [redacted] that I am scheduled for a foreign inspection & will not be back until the fourth week of November 2004. In addition, I told [redacted] that I will not be available to go back to the firm until after the holidays are over because I have to write three reports for my foreign inspection. This situation & the firm's attitude were also relayed to Kathy Anderson.

On January 3, 2005, I received a copy of a letter, dated October 27, 2004 (Exhibit #6) sent by [redacted] from MABP to Mr. Barry Cadden. I also received a copy of Mr. Cadden's response letter to [redacted] dated November 8, 2004 (Exhibit #7) stating the corrective actions to be undertaken/undertaken by NECC. I showed these letters to [redacted]Ann Simoneau & my plan to close out the inspection.

[redacted] was able to obtain a log of Trypan Blue that was compounded & dispensed from January 12, 2004 to September 28, 2004 (Exhibit #8), with some prescriptions attached. These prescriptions are examples of patients in the log who were dispensed at least more than one or two vials of Trypan Blue.

On January 18, 2005, I notified [redacted] that we do not have to go back to NECC to close out the inspection & that I'm doing it over the phone.

On January 19, 2005, I telephoned Mr. Barry Cadden & informed him that we are closing out the inspection based on his response letter to [redacted] of the MABP, indicating his plan of corrective actions, which will also be forwarded to headquarters. Before our conversation ended, Mr. Cadden asked me, "Do you think headquarters knew that Trypan Blue would be approved before the assignment was issued?" I said I really don't know. Our conversation ended at this point & the inspection was ended.

ATTACHMENT:

Assignment from Compounding Team Leader, HFD-316
FDA-482,Notice of Inspection

EXHIBITS:

#1. Label of Trypan Blue PF 0.1% Injectable I ML vial
#2. Labeling of Trypan Blue used for shipment
#3. Certificate of Analysis for Trypan Blue LOT #C107217 from PCC
#4. Log of Trypan Blue Compounded & Dispensed (9/24-28/04)
#5. Responses to questions on assignment sent by Mr. Conigliaro, dated October 1, 2004
#6. Letter sent by Mr. James Emery from MABP to Mr. Barry Cadden, dated October 27, 2004
#7. Response letter sent by Mr. Barry Cadden, dated November 8, 2004, to Mr. James Emery, MABP
#8. Log of Trypan Blue compounded & dispensed from January 12 – September 28, 2004

[redacted]
NWE-DO

cc: Ann Simoneau, Compliance Officer
NWE-DO

MDPH-Division of Health Professions Licensure
INVESTIGATION REPORT
Page 1 of 7

Licensee Name: Barry Cadden **Docket No: DS 05-040**
License Number: PH 21239 **DS 2848**
Priority Code: 2 Received by DHPL: 11/23/04 Docket Opened: 11/23/04
Assigned: 11/23/04
Investigator Name: James Emery- Health Care Investigator
Supervisor Name: Leslie Doyle - Program Coordinator

SECTION I: Demographics and History

A. **LICENSEE INFORMATION:**

1. **Name of Licensee/Respondent:** Barry Cadden
2. **Address of Record:** [redacted]
3. **Current Address:** [redacted]
4. **Phone Number(s): Home** N/A **Cell (N/A) Business (N/A) Fax (N/A)**
   Licensee/Respondent Date of Birth: [redacted]
5. **License Type & No.:** PH 21239 **Current Status:** C **Exp. Date:** 12/31/06
6. **Original Date of Issuance:** 10/9/90
7. **Record of Standing Attached:** Yes
8. **Name of Educational Institution Attended:** University of RI
   Date of Graduation: 1990

B. **OTHER MASSACHUSETTS LICENSES HELD:** None
1. **Profession/Trade:**
2. **License No.** **Current Status:** **Exp. Date:** / /
3. **Prior Discipline (explain):** N
4. **Certified Documentation Attached:** ☐ Yes No

C. **NON-MASSACHUSETTS LICENSES HELD:** None
1. **Profession / Trade:**
2. **License No.** **Current Status:** **Exp. Date:** / /
3. **Prior Discipline (explain):**
4. **Certified Documentation Attached:** ☐ Yes ☐ No

D. **LICENSEE'S EMPLOYMENT INFORMATION:**
1. **Current Employer:** New England Compounding Center
2. **Address:** 697 Waverly St Framingham, MA 01702
3. **Telephone Number:** 508 820 0606

SECTION II: Interviews, Complainant Info & Index of Materials/Documents

A. **INTERVIEWS CONDUCTED:** List below and include labeled interview notes in case file

Individuals Interviewed (name/title)	**When/Where?** (dates/time of day)	**Type Interview** (in-person/phone)	**Contact Information** (phone, address, business)
1.			
2.			
3.			
4.			
5.			

MDPH-Division of Health Professions Licensure
INVESTIGATION REPORT

Licensee Name: Barry Cadden
License Number: PH 21239
Docket No: DS 05-040
DS 2848

B. WITNESSES NOT AVAILABLE FOR INTERVIEW: Document attempts in case file

Individuals	Contact Information (phone, address, business)	Attempt(s) to contact (dates, times)
1.		
2.		
3.		

E. COMPLAINANT INFORMATION:
1. NAME OF COMPLAINANT: Board of Pharmacy
2. ADDRESS: 239 Causeway St, Boston, MA 02114
3. PHONE NO: (617) 727 0086 CELL PHONE: (N/A)

D. INDEX OF MATERIALS/DOCUMENTS: Label documents/materials as noted below in order of presentation in the file

ITEM 1:Complaint
ITEM 2:Record of Standing
ITEM 3: Staff assignment 05-006
ITEM 4: NECC Order Form
ITEM 5:
ITEM 6:
ITEM 7:
ITEM 8:

SECTION III: Investigation Summary

Allegation of Complaint: Failure to adhere to the standards of practice, specifically compounding and dispensing of a medication without a valid prescription (non patient specific)

Describe documentation/facts that support allegations:

Staff assignment presented at Board meeting of 11/23/04. Board voted to bring staff assignment to formal complaint.

Describe documentation/facts that do not support allegations: None

TYPE OF ERROR:

___ WRONG STRENGTH
___ WRONG DRUG
___ WRONG DIRECTIONS
___ WRONG PATIENT
___ OTHER - blisterpak information was incorrect
___ DRUG / DIRECTIONS DOSE PRESCRIBED
___ DRUG / DIRECTIONS DOSE DISPENSED
___ DISPENSED RX LABEL CORRECT
___ DISPENSED LABEL INCORRECT
___ NEW PRESCRIPTION
___ REFILL PRESCRIPTION
___ INGESTION OCCURRED

MDPH-Division of Health Professions Licensure

INVESTIGATION REPORT

Licensee Name: Barry Cadden **Docket No: DS 05-040**
License Number: PH 21239 **DS 2848**

_X_ OTHER- Failure to adhere to the standards of practice, specifically compounding and dispensing of a medication without a valid prescription (non patient specific)

*****Board should review item #4. NECC Order Form provided in response. Form is non-compliant by Board determination. NECC was notified by telephone (Greg Conigliaro) that the form currently used is non-compliant and must stop the use of this form immediately.**

PATIENT STATUS:

A. Setting Where Alleged Incident/Conduct Occurred:

1. **Current Employer:** New England Compounding Center
2. **Address:** 697 Waverly St Framingham, MA 01702
3. **Telephone Number:** 508 820 0606
   Contact and Title: Barry Cadden, Manager of Record

1. **If employed by another entity other than where the alleged incident occurred:**
   Name: N/A
   Address N/A
   Phone No: N/A
   Contact Person: N/A
   Contact's Title: N/A
   Licensee's Supervisor (if applicable give name): N/A
   Phone number

B. Attorney of Record: NA

1. **Name of Attorney:**
2. **Name of Firm:**
3. **Address:**
4. **Phone No(s).** Fax No. ( )

D. Investigator's Activities and Findings:
Describe - who, what, where, when, and why.

1. Complainant's allegation: Failure to adhere to the standards of practice, specifically compounding and dispensing of a medication without a valid prescription (non patient specific)

2. Licensee's response: A review of the same documentation provided to you does show what would appear to be incorrect or repetitive names being provided by several of our prescribing physicians. We have instituted a new Standard Operating Procedure for the Quality Check and Vetting of Patient Names, which should eliminate these inconsistencies in the future. This new SOP is included herein at "Attachment A." Additionally, per Leslie Doyle's last inspection, the newest version of the Prescription Order Form, included herein as "Attachment B," specifically includes a Verification Step

at the bottom which requires a Registered Pharmacist or designee, to verify all items shown on the Patient Order Form, including patient names.

Summary of events from medical records:

4. **Describe any information learned or submitted that does not support the Allegation:** None

5. **Describe any information requested and not received:** None

6. **Other Information:** N/A
Patient Record:
Charting: ☐ Perio ☐ Hard Tissue ☐ Soft Tissue
☐ Medical History ☐ Treatment Plan ☐ Informed Consent
☐ Radiographs ☐ Anesthesia Record ☐ CPR Certification
☐ On-Site Inspection (optional)

7. **Describe any exhibits not in case file (study models, radiographs, tapes, etc.). Describe location and with whom.**
NA

8. **List other state/federal or municipal agencies involved or also investigating this case and include contact information (name, address, telephone no.)**

E. COMPLAINT HISTORY

1. **Companion Complaints:** (list docket numbers, allegations, status, and disposition)

2. **Complaint Pending Board:** None

3. **Complaints Pending Prosecutions:** None

4. **Related Complaints:** (list docket numbers, allegations, status, and disposition) None

5. **Prior Complaints: (list docket numbers, allegations, status, and disposition)**

20021211DS036- Unprofessional conduct-Dismissed, advisory letter
20030212DS055- Failure to adhere to the standards of practice-PB
20030226DS060- Failure to adhere to the standards of practice, Dismissed, Advisory letter
20040504DS062-Unethical conduct- Dismissed, Advisory letter

19990330PH066-Unprofessional Conduct-Dismissed, informal reprimand
20021211PH042-Unprofessional Conduct-Dismissed, Advisory letter
20030212PH066- Failure to adhere to the standards of practice-PB
20030226PH070- Failure to adhere to the standards of practice-Dismissed, Advisory letter

MDPH-Division of Health Professions Licensure

INVESTIGATION REPORT

Licensee Name: Barry Cadden Docket No: DS 05-040
License Number: PH 21239 DS 2848

6. Criminal Offender Records Information Check (CORI) been performed? Yes
Include certified copies of judgments: No

F. In your opinion should case go to Medical Error Triage: No
Explain:

G. Summary of alleged violation(s) of regulation/statutes (include description of licensee's actions that constitute the basis of the violation(s).

H. Staff Recommendation(s):

- ☐ Dismissal with Prejudice: No Violation
- ☐ Dismissal without Prejudice
- ☐ Lack of Sufficient Evidence
- X Dismissal with Advisory Letter
- ☐ Stayed Probation
  ☐ Terms:
- ☐ Reprimand
- ☐ Probation
  ☐ Terms:
- ☐ Censure
- ☐ Offer Voluntary Surrender
  ☐ Terms:
- ☐ Summary Suspension
  ☐ Terms:
- ☐ Revocation
  ☐ Terms:

CONTINUING EDUCATION REQUIREMENTS:
Enclosed

OTHER TERMS: MPRS evaluation

INVESTIGATOR SIGNATURE:_____DATE:_____
SUPERVISOR SIGNATURE: _____DATE:_____

****

Complaint Committee Decision/Recommendation: CC Meeting Date:

Re: Staff recommendation:
☐ CC Agrees ☐ CC Disagrees (making the following recommendation)

- ☐ Dismissal with Prejudice: No Violation
- ☐ Dismissal without Prejudice
- ☐ Lack of Sufficient Evidence
- ☐ Dismissal with Advisory Letter
- ☐ Stayed Probation
  ☐ Terms:
- ☐ Probation
  ☐ Terms:
- ☐ Censure
- ☐ Offer Voluntary Surrender
  ☐ Terms:
- ☐ Summary Suspension
  ☐ Terms:

MDPH-Division of Health Professions Licensure

INVESTIGATION REPORT

Licensee Name: Barry Cadden
License Number: PH 21239
☐ Reprimand

Docket No: DS 05-040
DS 2848
☐ Revocation
☐ Terms:

CONTINUING EDUCATION REQUIREMENTS:

OTHER TERMS:

Summary of alleged violation(s) of regulation/statutes (include description of licensee's actions that constitute the basis of the violation(s)):

Notes:

****

BOARD'S Decision/Recommendation: Board Meeting Date:

Re: Staff or/ CC recommendation:

☐ Board Agrees ☐ Board Disagrees (making the following recommendation)

☐ Dismissal with Prejudice:
☐ No Violation

☐ Probation
☐ Terms:

☐ Dismissal without prejudice
☐ Lack of Sufficient Evidence
☐ Dismissal with Advisory Letter

☐ Censure

☐ Offer Voluntary Surrender
☐ Terms:

☐ Stayed Probation
☐ Terms:

☐ Summary Suspension
☐ Terms:

☐ Reprimand

☐ Revocation
☐ Terms:

CONTINUING EDUCATION REQUIREMENTS:

OTHER TERMS:

Summary of alleged violation(s) of regulation/statutes (include description of licensee's actions that form the basis of the violation(s)):

Notes:

Votes:

MDPH-Division of Health Professions Licensure

INVESTIGATION REPORT

Licensee Name: Barry Cadden
License Number: PH 21239

Docket No: DS 05-040
DS 2848

****

DISPOSITION OF CASE:

Refer to Board Counsel / Date:

Refer to Prosecution / Date:

Other

BOARD OF REGISTRATION IN PHARMACY File Review

Summary of Outstanding complaints

Allegation.

Licensee response:

Licensee:
Recommended action (choose one):

1)	STAFF ASSIGNMENT BRNG TO COMPLAINT:	✓	2)	INFORMAL CONFERENCE	
3)	ADVISORY LETTER	✓	4)	DISMISS	
5)	NO VIOLATION – DISMISS		6)	LACK OF EVIDENCE -DISMISS	
7)	LACK OF JURISDICTION – DISMISS		8)	DISMISS - without prejudice	
9)	ADDITIONAL CEU'S – DISMISS		10)	INVESTIGATOR – FOLLOW-	
11)	Licensee is offered to enter MPRS:				

Board of Registration in Pharmacy- Reviewed by: (two signatures required)

James Devita - RPH President: _____ DATE _____

Karen Ryle - RPH Secretary: _____ DATE _____

Harold Spatt - RPH Member: _____ DATE _____

Dr. Donald Accetta: Member _____ DATE _____

Joel Berman - RPH Member: _____ DATE 11/23/04

George Cayer - RPH Member: _____ DATE 11/23/04

William Gouveia RPH Member: _____ DATE _____

Sophia Pasedis RPH Member: _____ DATE _____

Marilyn Barron: Public Member _____ DATE _____

Steve Budish Public Member _____ DATE _____

COMMONWEALTH OF MASSACHUSETTS

SUFFOLK COUNTY

BOARD OF REGISTRATION IN PHARMACY

In the Matter of	
NEW ENGLAND COMPOUNDING CENTER	Docket Nos. DS-03-055
Registration No. 2848	PH-03-066
BARRY J. CADDEN, R.Ph.	DS-05-040
License No. 21239	

CONSENT AGREEMENT

The Board of Registration in Pharmacy ("Board") and NEW ENGLAND COMPOUNDING CENTER ("NECC") (Pharmacy Registration No. 2848), located at 697 Waverly Road, in Framingham, Massachusetts ("Registrant"), and BARRY J. CADDEN, R.Ph. ("Licensee") Pharmacist License No. 21239 and Manager of Record of Registrant, do hereby stipulate and agree that the following information shall be entered into and become a permanent part of the files of Registrant and Licensee which are maintained by the Board:

1. The parties enter into this Consent Agreement ("Agreement") to resolve disputed matters arising out of the complaints pending against Registrant and Licensee, respectively, as Docket Nos. DS-03-055, PH-03-066 and DS-05-040 ("Complaints").

2. The Registrant, Licensee and the Board stipulate and agree that this Agreement is in settlement of complaints relating to an adverse event complaint report investigated by the United States Food and Drug Administration for methylprednisolone acetate preservative free 80 mg/ml suspension, and concerning the dispensing of Trypan Blue without a valid prescription ("the Complaints").

3. The Registrant, Licensee and the Board acknowledge that this Agreement is a nondisciplinary agreement not reported to the National Association of State Boards of Pharmacy or other outside report agencies, except that the Licensee's failure to fulfill the requirements of paragraph 5 may result in the imposition of discipline by the Board.

4. In order to resolve these matters without further proceedings before the Board, the Registrant, the Licensee, and the Board agree that on the date of the execution of this Agreement by the Board ("Effective Date") the Board will order that the Licensee be placed on Probation for a Period of One (1) Year, and the probation order will be

Stayed for one (1) year from the Effective Date of this Agreement ("the Stay").

5. The Registrant and the Licensee agree as follows:

(a) Within 45 days from the Effective Date of this Agreement, the Registrant and Licensee shall provide documentation satisfactory to the Board that Board-approved evaluator: Pharmacy Support, Inc. ("PSI" or "Evaluator"), at the expense of the Registrant and Licensee, has conducted an inspection of and prepared a written report analyzing Registrant's compounding practices and compliance with United States Pharmacopeia Standard 795 – Non-Sterile Compounding Procedures and USP Standard 797 – Sterile Compounding Procedures, in accordance with 247 CMR 9.01(3)("USP Standards"), with any recommendations for revisions to practice for compliance with USP Standards ("the First Report"). The inspection shall include consideration of, but not be limited to:

i. Sterile Environmental Design
ii. Quality Assurance Program
iii. Media Fills (operator qualification/process validation)
iv. Environmental Monitoring
v. Cleaning and Sanitizing Program
vi. Training Records
vii. Process Control
viii. Equipment
ix. Finished Preparation Testing
x. Adverse Event Records

(b) The Registrant and Licensee will arrange for the Evaluator to provide a copy of the First Report as described in Paragraph 5(a) directly to the Board within fourteen days of the inspection.

(c) The Registrant and Licensee will implement all recommendations made by the Evaluator within 90 days of the Effective Date of this Agreement. The Registrant and Licensee must petition and receive the approval of the Board to exempt or postpone implementation of any particular recommendation.

(d) Within six months of the Effective Date of this Agreement, the Registrant and Licensee shall provide documentation satisfactory to the Board that the Evaluator, at the expense of the Registrant and Licensee, has conducted a second inspection of Registrant and prepared a written report after an analysis as described in Paragraph (5) above, and further, as to whether the recommendations made by the Evaluator in the First Report have been implemented ("the Second Report").

(e) The Registrant and Licensee will arrange for the Evaluator to provide a copy of the Second Report as described in Paragraph 5(d) directly to the Board within fourteen days of the inspection.

(f) The Registrant and Licensee will update Standard Operating Procedures on a biannual

basis.

(g) The Registrant and Licensee will keep a written report of each adverse event reported and make such reports available for review by the Board upon request.

6. If the Registrant and Licensee successfully complete the requirements of paragraph 5, its registration and his license will not be placed on probation.

7. If the Registrant and the Licensee fail to successfully complete the requirements of paragraph 5, the Stay will be withdrawn by the Board and the Board's order of Probation for a Period of One (1) Year ("Probation") will be imposed upon the Registrant and Licensee without the necessity of additional proceedings pursuant to G. L. c. 30A. The terms and conditions of Probation will be determined by the Board at that time and may include, but not be limited to practice restrictions, monitoring conditions, appearances before the Board, and continuing education and training.

8. This Agreement and its contents shall be incorporated into the records maintained by the Board. This Agreement and its contents are matters of public record, and are subject to disclosure without limitation to the public and equivalent state licensing boards.

9. The Board agrees that in return for the execution and fulfillment of the requirements of this Agreement by the Registrant and Licensee, the Board will not advance the prosecution of the Registrant and Licensee pursuant to the Complaints; any and all other rights of the Board to take action within the scope of its authority are expressly reserved.

10. The Registrant and Licensee understand and agree that the failure to accept the terms of this Agreement shall nullify the representations contained herein, and permit the Board to initiate formal adjudicatory action under the State Administrative Procedure Act, G.L. c. 30A, and the Standard Adjudicatory Rules of Practice and Procedure, 801 CMR 1.00 *et. seq.*

11. The Registrant and Licensee understand and agree that the decision to enter into this Agreement and to accept the terms and conditions herein described is a final act and is not subject to reconsideration or judicial review.

12. The Registrant and Licensee state legal counsel has been consulted in connection with the decision to enter into this Agreement and if not, that there was an opportunity to do so.

13. The Registrant and Licensee certify this document entitled "Consent Agreement" has been read. The Registrant and Licensee understand that, by executing this Agreement, the Registrant and Licensee are waiving any right to a formal hearing with rights to confront and cross-examine witnesses, to call witnesses, to present evidence, to testify on its own behalf, to contest the allegations, to present oral argument, to appeal to court in the event of an adverse ruling, and all other rights set forth in G.L. c. 30A and 801 CMR 1.01 *et seq.*

NEW ENGLAND
COMPOUNDING CENTER

By: Barry J. Cadden
Barry J. Cadden, R.Ph.
Director of Pharmacy

Date: 1/5/06

Barry J. Cadden
Barry J. Cadden, R.Ph.
Manager of Record
Date: 1/5/06

BOARD OF REGISTRATION
IN PHARMACY

By: Karen Ryle
Karen Ryle, R.Ph., M.S.
President

Effective Date: 1/10/06

Board Dec. No. 1210, 1211
Cert Mail No.

DEPARTMENT OF HEALTH & HUMAN SERVICES
Food and Drug Administration
New England District

W.L-File

One Montvale Avenue
Stoneham, Massachusetts 02180
(781) 596-7700
FAX: (781) 596-7895

WARNING LETTER
NWE-06-07W

VIA FEDERAL EXPRESS

December 4, 2006

Barry J. Cadden, Director of Pharmacy and Owner
New England Compounding Center
697 Waverly Street
Framingham, MA 01702

Dear Mr. Cadden:

On September 23, 2004, investigators from the U.S. Food and Drug Administration (FDA) and the Massachusetts Board of Pharmacy inspected your firm, located at 697 Waverly Street, Framingham, Massachusetts. On January 19, 2005, the inspection was completed. This inspection revealed that your firm compounds human prescription drugs in various dosage forms and strengths.

We acknowledge the receipt of your October 1, 2004, letter addressed to FDA's New England District Office, concerning questions presented during the referenced inspection.

FDA's position is that the Federal Food, Drug, and Cosmetic Act (FDCA) establishes agency jurisdiction over "new drugs," including compounded drugs. FDA's view that compounded drugs are "new drugs" within the meaning of 21 U.S.C. § 321(p), because they are not "generally recognized, among experts . . . as safe and effective," is supported by substantial judicial authority. *See Weinberger v. Hynson, Westcott & Dunning,* 412 U.S. 609, 619, 629-30 (1973) (explaining the definition of "new drug"); *Prof'ls & Patients for Customized Care v. Shalala,* 56 F.3d 592, 593 n.3 (5th Cir. 1995) (the FDCA does not expressly exempt pharmacies or compounded drugs from its new drug provisions); *In the Matter of Establishment Inspection of: Wedgewood Village Pharmacy,* 270 F. Supp. 2d 525, 543-44 (D.N.J. 2003), *aff'd, Wedgewood Village Pharmacy v. United States,* 421 F.3d 263, 269 (3d Cir. 2005) ("The FDCA contains provisions with explicit exemptions from the new drug . . . provisions. Neither pharmacies nor compounded drugs are expressly exempted."). FDA maintains that, because they are "new drugs" under the FDCA, compounded drugs may not be introduced into interstate commerce without FDA approval.

The drugs that pharmacists compound are not FDA-approved, and lack an FDA finding of safety and efficacy. However, FDA has long recognized the important public health function served by traditional pharmacy compounding. FDA regards traditional compounding as the extemporaneous combining, mixing, or altering of ingredients by a pharmacist in response to a

physician's prescription to create a medication tailored to the specialized needs of an individual patient. *See Thompson v. Western States Medical Center*, 535 U.S. 357, 360-61 (2002). Traditional compounding typically is used to prepare medications that are not available commercially, such as a drug for a patient who is allergic to an ingredient in a mass-produced product, or diluted dosages for children.

Through the exercise of enforcement discretion, FDA historically has not taken enforcement actions against pharmacies engaged in traditional pharmacy compounding. Rather, FDA has directed its enforcement resources against establishments whose activities raise the kinds of concerns normally associated with a drug manufacturer and whose compounding practices result in significant violations of the new drug, adulteration, or misbranding provisions of the FDCA.

FDA's current enforcement policy with respect to pharmacy compounding is articulated in Compliance Policy Guide (CPG), section 460.200 ["Pharmacy Compounding"], issued by FDA on May 29, 2002 (*see Notice of Availability*, 67 *Fed. Reg.* 39,409 (June 7, 2002)).[1] The CPG identifies factors that the Agency considers in deciding whether to initiate enforcement action with respect to compounding. These factors help differentiate the traditional practice of pharmacy compounding from the manufacture of unapproved new drugs. They further address compounding practices that result in significant violations of the new drug, adulteration, or misbranding provisions of the FDCA. These factors include considering whether a firm compounds finished drugs from bulk active ingredients that are not components of FDA-approved drugs, without an FDA sanctioned investigational new drug application (IND). The factors in the CPG are not intended to be exhaustive and other factors may also be appropriate for consideration.

1. Copies of Commercially Available Drug Products:

It has come to our attention that you are compounding trypan blue ophthalmic products. During the inspection at your firm, you advised an investigator from FDA's New England District Office that the trypan blue products that your firm compounds are devices. FDA classifies trypan blue products as drugs, not devices. Further, on December 16, 2004, trypan blue ophthalmic solution was approved by FDA and it is commercially available. As stated in the CPG, FDA will not exercise its enforcement discretion for the compounding of copies of commercially available FDA-approved products, including this one.

We have also learned that your firm may be compounding 20% aminolevulinic acid solution (ALA). Please note that there is a commercially available, FDA-approved aminolevulinic acid solution 20%. Like compounded trypan blue, FDA regards compounded 20% aminolevulinic acid solution as a copy of commercially available drug.

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[1] Although Section 503A of the FDCA (21 U.S.C. § 353a) addresses pharmacy compounding, this provision was invalidated by the Supreme Court's ruling in *Thompson v. Western States Medical Center*, 535 U.S. 357 (2002), that Section 503A included unconstitutional restrictions on commercial speech. And those restrictions could not be severed from the rest of 503A. In *Thompson v. Western States Medical Center*, 535 U.S. 357 (20020), the Supreme Court affirmed the Ninth Circuit ruling that the provisions in question violated the First Amendment.

FDA does not sanction the compounding of copies of FDA-approved, commercially available drugs and the agency will not exercise its enforcement discretion regarding the trypan blue and ALA products compounded by your firm.

All products compounded by your firm containing trypan blue or ALA are drugs within the meaning of section 201(g) of the FDCA (21 U.S.C. § 321(g)). These products are misbranded under section 502(f)(1) of the FDCA (21 U.S.C. § 352(f)(1)) in that their labeling fails to bear adequate directions for their use. They are not exempt from this requirement under 21 CFR § 201.115 because they are new drugs within the meaning of section 201(p) of the FDCA and they lack approved applications filed pursuant to section 505 of the FDCA (21 U.S.C. § 355).

2. Anesthetic Drug Products:

Equally serious, your firm's promotional materials reveal that it offers to compound "Extra Strength Triple Anesthetic Cream" which contains 20% benzocaine, 6% lidocaine, and 4% tetracaine. Like a manufacturer, you have developed a standardized anesthetic drug product that you sell under the name "Extra Strength Triple Anesthetic cream." Further, you generate sales by giving physicians "courtesy prescriptions" (i.e., free samples). These actions are not consistent with the traditional practice of pharmacy compounding, in which pharmacists extemporaneously compound reasonable quantities of drugs upon receipt of valid prescriptions from licensed practitioners to meet the unique medical needs of individual patients.

Moreover, the agency is concerned with the public health risks associated with the compounding of "Extra Strength Triple Anesthetic Cream." There have been at least two non-fatal reactions and two deaths attributed to the use of compounded topical local anesthetic creams containing high doses of local anesthetics. Local anesthetics, like "Extra Strength Triple Anesthetic Cream," may be toxic at high dosages, and this toxicity can be additive. Further, there is a narrow difference between the optimal therapeutic dose of these products and the doses at which they become toxic, i.e. they have low therapeutic index.

Adverse events consistent with high systemic exposures to these products include seizures and cardiac arrhythmias. Specifically, risk of systemic adverse events from tetracaine products includes (1) a systemic allergic response to p-aminobenzoic acid (PABA) which, at worst, could lead to cardiac arrest; or (2) excessive systemic absorption following repetitive or extensive application, especially for a 4% product, which could ultimately lead to convulsions. Tetracaine is associated with a higher incidence of allergic reactions than other anesthetics, such as lidocaine. The risk of systemic toxicity is greatest in small children and in patients with pre-existing heart disease. Factors that may increase systemic exposure are time and surface area of the exposure, particularly when the area of application is covered by an occlusive dressing. Benzocaine has an additional toxicity not seen with lidocaine, methemoglobinemia, an acquired decrease in the oxygen-carrying capacity of the red blood cells. Further, patients with severe hepatic disease are at greater risk of developing toxic plasma concentrations of local anesthetics because of their inability to metabolize them.

The Extra Strength Triple Anesthetic Cream compounded by your firm is a drug within the meaning of section 201(g) of the FDCA (21 U.S.C. § 321(g)). This product is misbranded under section 502(f)(1) of the FDCA (21 U.S.C. § 352(f)(1)) in that its labeling fails to bear adequate directions for its use. It is not exempt from this requirement under 21 CFR § 201.115, because it is a new drug within the meaning of section 201(p) of the FDCA that lacks an approved application filed pursuant to section 505 of the FDCA (21 U.S.C. § 355).

Depending on its labeling, this product may also violate section 502(a) of the FDCA (21 U.S.C. § 352(a)). A drug or device is misbranded under section 502(a) if its labeling is false and misleading in any particular (e.g., if the labeling for your local anesthetic products fails to reveal the consequences that may result from the use of the product as a local anesthetic).

3. Repackaging:

Additionally, we are in receipt of a complaint alleging that you are repackaging the approved injectable drug, Avastin, into syringes for subsequent promotion and sale to health professionals. Avastin is unpreserved and is packaged and labeled in 4 and 16 ml single-use glass vials. The labeled precautions include "discard any unused portion left in a vial . . . ."

Each step in the manufacture and processing of a new drug or antibiotic, from handling of raw ingredients to final packaging, must be approved by FDA, whether carried out by the original manufacturer or by some subsequent handler or repacker of the product. Pharmacists are not exempt from these statutory requirements. Generally, the agency regards mixing, packaging, and other manipulations of approved drugs by licensed pharmacists, consistent with the approved labeling of the product, as an approved use of the product if conducted within the practice of pharmacy, i.e., filling prescriptions for identified patients. However, processing and repacking (including repackaging) of approved drugs is beyond the practice of pharmacy and is thus subject to the Act's premarket approval requirements.

The agency has an established policy, articulated in Compliance Policy Guide Sec. 446.100, Regulatory Action Regarding Approved New Drugs and Antibiotic Drug Products Subjected to Additional Processing or other Manipulations (CPG 7132c.06) (copy enclosed), concerning the manipulation of approved sterile drug products outside the scope of the FDA-approval. FDA is particularly concerned about the manipulation of sterile products when a sterile container is opened or otherwise entered to conduct manipulations. The moment a sterile container is opened and manipulated, a quality standard (sterility) is destroyed and previous studies supporting the standard are compromised and are no longer valid. We are especially concerned with the potential microbial contamination associated with splitting Avastin -- a single-use, preservative-free, vial -- into multiple doses. When used intravitreally, microbes could cause endophthalmitis, which has a high probability for significant vision loss. The absence of control over storage, and delays before use after repackaging, only exacerbate these concerns.

Avastin is approved for use in the treatment of colorectal cancers. The text of your alleged promotional material offers this drug to ophthalmologists. Avastin has no approved indications for use in the eye. As such, your firm is distributing an unapproved new drug in violation of section 505 of the FDCA. Because the product lacks adequate labeling for its intended use (see 21 CFR § 201.128) your firm is also distributing a misbranded drug in violation of section 502(f)(1) of the FDCA (21 U.S.C. § 352(f)(1)).

Also, please note that, under section 301(a) of the FDCA (21 U.S.C. § 331(a)), the introduction or delivery for introduction into interstate commerce of any drug that is misbranded is prohibited. Under section 301(d) of the FDCA (21 U.S.C. § 331(d)), the introduction or delivery for introduction into interstate commerce of a new drug that has not been approved under section 505 is also prohibited.

Further, we have been informed that, although your firm advises physicians that a prescription for an individually identified patient is necessary to receive compounded drugs, your firm has reportedly also told physicians' offices that using a staff member's name on the prescription would suffice. Drugs compounded in this manner are not compounded consistent with the CPG, and FDA will not exercise its enforcement discretion regarding those drugs.

The above violations are not intended to be an all-inclusive list of deficiencies. You should take prompt action to correct these deviations. Failure to promptly correct these deviations may result in additional regulatory action without further notice, including seizure or injunction against you and your firm. Federal agencies are routinely advised of the issuance of warning letters so that they may take this information into account when considering the award of government contracts.

Please notify this office in writing within 15 working days of receipt of this letter of any steps that you will take to correct the noted violations, including an explanation of the steps taken to prevent the recurrence of similar violations. If corrective action cannot be completed within 15 working days, please state the reason for the delay and the time within which the correction will be complete.

You should address your reply to this letter to the U.S. Food and Drug Administration, New England District Office, One Montvale Ave., 4th Floor, Stoneham, MA 02180, Attn: Ann Simoneau, Compliance Officer. If you have any further questions, please feel free to contact Ms. Simoneau at (781) 596-7732.

Sincerely,

Carl T. Costello
District Director
New England District Office

cc: Charles R. Young, RPH
Executive Director
Massachusetts State Board of Pharmacy
239 Causeway Street, 5th floor
Boston, MA 02114

New England Compounding Center
697 Waverly Street, Framingham, MA 01702
Tel: 800.994.6322 or 508.820.0606
Fax: 888.820.0583 or 508.820.1616 mail@neccrx.com

January 5, 2007

Ann Simoneau
Compliance Officer
U.S. Food and Drug Administration
New England District Office
One Montvale Avenue, 4th Floor
Stoneham, Massachusetts 02180

BY FACSIMILE & FEDEX

Re: Warning Letter to New England Compounding Center, NEW-06-07W

Dear Ms. Simoneau:

We are writing to respond to the Warning Letter issued to New England Compounding Center ("NECC") dated December 4, 2006. Thank you for extending our response due date to January 5, 2007. NECC is committed to complying with applicable laws and regulations and to ensuring high quality care for our patients. We appreciate the opportunity to clarify the nature of our pharmacy operations and to respond to the issues raised in the Warning Letter.

At the outset, we note that the Warning Letter is based on an inspection of NECC that started on September 23, 2004, approximately twenty-eight months ago, and ended on January 19, 2005, approximately twenty-three months ago. FDA has not contacted us since concluding the inspection. Some of the letter's assertions no longer apply to NECC's operations.

We have been advised by our counsel that the five most recent Warning Letters issued by FDA's New England District Office to non-pharmacy medical device and drug manufacturers were sent, on average, 110 days after the recipients' facilities had been inspected. The Warning Letter we received arrived 684 days after FDA's inspection of our pharmacy was completed. This twenty-three month delay is nearly a year and a half longer than the District's recent average response time. This prolonged gap between

inspection and Warning Letter does not comply with FDA's procedures, which establish that decisions to issue Warning Letters must be made in a timely fashion, because they are "the agency's principal means of notifying the regulated industry of violations and achieving prompt voluntary correction."[1] The Warning Letter also mentions FDA's concerns about potentially serious health risks associated with the misuse by physicians and patients of compounded topical anesthetic drug products. We take the welfare of our patients very seriously. We believe that FDA's nearly two year delay in issuing the Warning Letter contradicts FDA's rhetoric regarding the asserted risks associated with our compounded products.

The Warning Letter states that FDA believes that it has jurisdiction over compounded drugs because such drugs are "new drugs" within the meaning of Section 201(p) of the Food, Drug, and Cosmetic Act (FDC Act). The Warning Letter cites several court cases. However, it ignores the fact that the only federal court to have directly considered the issue recently rejected FDA's legal theory. In Medical Center Pharmacy v. Gonzales, the federal District Court for the District of Western Texas granted the plaintiff pharmacies' summary judgment on their "claim that compounded drugs do not fall under the [FDC Act's] new drug definitions."[2] The court based this conclusion on "relevant case and statutory law, as well as legislative intent."[3] We do not understand why the Warning Letter ignores the single most relevant judicial opinion.

The Warning Letter also refers to the Supreme Court's pharmacy compounding decision in Thompson v. Western States Medical Center,[4] but neglects to mention that the Medical Center Pharmacy court's opinion stated that "the language of Western States

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1 FDA, Regulatory Procedures Manual 4-10 (March 2006).

2 Med. Ctr. Pharmacy v. Gonzales, 451 F. Supp. 2d 854, 865 (W.D. Tex. 2006), appeal docketed, No. 06-51583 (5th Cir. Dec. 11, 2006).

3 Id. at 858.

4 535 U.S. 357 (2002).

demonstrates that compounding is a process that has been approved by the Supreme Court."[5] Accordingly, we believe that compounded drugs are not automatically new drugs.

Contrary to the Warning Letter's assertion, NECC does not compound copies of FDA-approved commercially available drugs, introduce unapproved new drugs into interstate commerce, does not need approved NDAs before dispensing its compounded medications, and does not process or repackage approved drugs in a manner that would subject us to FDA regulation. Nor are our compounded medications misbranded. NECC dispenses compounded medications upon the receipt of valid prescriptions. We are engaged in the practice of pharmacy and comply with the Massachusetts Board of Registration in Pharmacy's laws and rules. We engage in the kind of activity that the Medical Center Pharmacy court determined does not result in the introduction of new drugs into interstate commerce.

Copies of Commercially Available Drug Products

Your letter asserts that NECC is compounding trypan blue ophthalmic medications and 20% aminolevulinic acid solution (ALA), and that these medications are copies of commercially available, FDA-approved drugs. Without agreeing with the correctness of the Warning Letter's assertions, please note that we stopped filling prescriptions for trypan blue in August 2005 (16 months before the Warning Letter) and for ALA in May 2006 (7 months before the Warning Letter) for business reasons completely unrelated to the FDA's assertions.

Anesthetic Drug Products

The letter also asserts that NECC has developed a standardized line of topical anesthetic drug products. This is not the case. NECC compounds a number of different

[5] 451 F. Supp. 2d at 864.

topical anesthetic formulas containing a variety of component ratios. The formulation depends on the prescribing physicians' requests. Physicians do prescribe certain formulations more frequently than others, but these choices by physicians do not mean that NECC has developed a standardized formula and therefore acts as if it were a drug manufacturer. We compound solely in accordance with formulas determined by the prescribing physicians. Moreover, NECC compounds a small volume of topical anesthetic medications.

NECC currently uses the term "triple anesthetic cream," (not "extra strength triple anesthetic cream"), but only as a way to literally describe the compounded medication as a convenience to our prescribing physicians. The term is in no way trademarked or branded. Assigning names to formulas is common in pharmacy practice, and does not mean that a pharmacy is a manufacturer. Nonetheless, to address FDA's concerns on this point, should the FDA believe that our use of the term "triple anesthetic cream" is problematic, please advise and we will consider discontinuing that description of the compounded medication. As always, we will continue to require physicians to specify the desired chemical formulation in each patient-specific prescription.

The Warning Letter alleges that there are potentially serious health risks associated with the misuse of compounded local anesthetic products because of the potential for systemic toxicity. Virtually all drugs, including manufactured drugs, pose serious health risks if they are misused by physicians or patients.

The Warning Letter also states that the courtesy prescriptions NECC provides in limited circumstances constitute "free samples," and that this is inconsistent with the traditional practice of pharmacy compounding. Although we do provide a very small quantity of medications (less than ten per month) free of charge, we do so only upon receipt of a valid prescription from a licensed practitioner to meet the unique medical needs of a particular patient. The provision of a prescribed medication at no charge is within our rights and is certainly not inconsistent with the practice of pharmacy. Thus,

these are not samples as that term is defined in the Prescription Drug Marketing Act. A valid prescription does not become unlawful just because we do not charge the physician or patient. Should the FDA believe our position on this matter is incorrect, please advise.

Repackaging

The Warning Letter asserts that NECC's repacking of Avastin into syringes constitutes manufacturing. However, your letter also explains that "[g]enerally, the agency regards mixing, packaging, and other manipulations of approved drugs by licensed pharmacists, consistent with the approved labeling of the product, as an approved use of the product if conducted within the practice of pharmacy, i.e., filling prescriptions for identified patients."[6] This is precisely what we do. NECC's repacking activity constitutes the practice of pharmacy because we repackage Avastin only upon receipt of a valid, patient-specific prescription from a licensed practitioner. NECC also maintains an ongoing Quality Assurance Program including Sterile Compounding Standard Operating Procedures. All aspects of our sterile compounding and repacking operations were recently reviewed by an independent expert, who confirmed that NECC is in compliance with all aspects of U.S. Pharmacopoeia ("USP") 797. In fact, NECC is one of only several preferred compounding pharmacy vendors approved nationwide by Genentech, the manufacturer of Avastin, to perform patient-specific repackaging services. This preferred vendor status was only awarded by Genentech after careful consideration of NECC's capabilities and track record in the performance of patient-specific compounding/repackaging services.

The Warning Letter alleges that NECC promotes Avastin for unapproved ophthalmologic uses. However, NECC does not promote Avastin for any particular uses but rather only promotes our own ability to compound representative medications to licensed practitioners for their patients. The physician's decision to prescribe a drug for

---

[6] Warning Letter at 4.

an off-label use, within the scope of the practice of medicine, does not cause our repackaging to be improper.

Finally, the Warning Letter states that NECC "reportedly" told physicians that we would fill prescriptions written in the name of a staff member rather than in the name of an actual patient. This allegation contradicts all of our standard operating procedures. NECC has not made such a representation to anyone, and has no idea how or why FDA arrived at this allegation. Should the FDA have specific knowledge of anyone on our staff making such an assertion to any physician, please provide same and we will address the matter immediately.

We believe that this response to the December 4th Warning Letter addresses FDA's concerns in full. We understand that FDA has a policy whereby responses to Warning Letters will be posted on the FDA website at the Warning Letter recipient's request. We therefore ask that this letter be posted on the FDA's website. We further request, of course, that FDA redact all confidential business information and all other information that is otherwise exempt from public disclosure under the Freedom of Information Act before either posting this response on the website or releasing it in response to a FOI request. We also ask that you consult with us about the FDA's proposed redactions before posting or otherwise publicly releasing the letter.

Thank you, again, for your consideration.

Sincerely,

NEW ENGLAND COMPOUNDING CENTER

Barry Cadden, RPh
Director of Pharmacy

cc James D. Coffey, RPh
Interim Executive Director, MA BOP
Counsel

DEPARTMENT OF HEALTH & HUMAN SERVICES
Food and Drug Administration
New England District

W-L-File

One Montvale Avenue
Stoneham, Massachusetts 02180
(781) 596-7700
FAX: (781) 596-7895

October 31, 2008

Mr. Barry J. Cadden, Director and Pharmacy Owner
New England Compounding Center
697 Waverly St.
Framingham, MA 01702

Dear Mr. Cadden:

This letter replies to your January 5, 2007 response to an FDA Warning Letter issued to your firm on December 4, 2006. We acknowledge and apologize for the significant delay in this correspondence.

Your letter asserts that the unapproved drug and misbranding charges in the Warning Letter do not apply because of the decision in *Medical Center Pharmacy v. Gonzales*, 451 F. Supp. 2d 854 (W.D. Tex. 2006). You also state that your firm engages in "the kind of activity that the *Medical Center Pharmacy* court determined does not result in the introduction of new drugs into interstate commerce."

As stated in the Warning Letter, FDA's position is that the Federal Food, Drug, and Cosmetic Act (FDCA) establishes agency jurisdiction over "new drugs," including compounded drugs. FDA's view is that compounded drugs are "new drugs" within the meaning of 21 U.S.C. § 321(p), because they are not "generally recognized, among experts . . . as safe and effective" for their labeled uses. *See Weinberger v. Hynson, Westcott & Dunning*, 412 U.S. 609, 619, 629-30 (1973) (explaining the definition of "new drug"). There is substantial judicial authority supporting FDA's position that compounded drugs are not exempt from the new drug definition. *See Professionals & Patients for Customized Care v. Shalala*, 56 F.3d 592, 593 n.3 (5th Cir. 1995) ("Although the [FDCA] does not expressly exempt 'pharmacies' or 'compounded drugs' from the new drug ... provisions, the FDA as a matter of policy has not historically brought enforcement actions against pharmacies engaged in traditional compounding."); *In the Matter of Establishment Inspection of: Wedgewood Village Pharmacy*, 270 F. Supp. 2d 525, 543-44 (D.N.J. 2003), *aff'd, Wedgewood Village Pharmacy v. United States*, 421 F.3d 263, 269 (3d Cir. 2005) ("The FDCA contains provisions with explicit exemptions from the new drug . . . provisions. Neither pharmacies nor compounded drugs are expressly exempted."). FDA maintains that, because they are "new drugs"

under the FDCA, compounded drugs may not be introduced into interstate commerce without FDA approval.

As to your argument based on *Medical Center Pharmacy v. Gonzales*, 451 F. Supp. 2d 854 (W.D. Tex. 2006), on July 18, 2008, the United States Court of Appeals for the Fifth Circuit issued a ruling in the case on appeal. *Medical Center Pharmacy v. Mukasey*, 536 F. 3d 383 (5th Cir. 2008). The Fifth Circuit rejected the finding by the United States District Court for the Western District of Texas that compounded drugs are exempt from the definition of "new drugs" in the FDCA. The Fifth Circuit concluded instead that compounded drugs are "new drugs." The court also ruled on the severability of advertising prohibitions in section 503A of the FDCA, which were found unconstitutional in a prior Supreme Court decision, *Thompson v. Western States Medical Center*, 535 U.S. 357 (2002).[1] The Fifth Circuit held that the restrictions on commercial speech in section 503A of the FDCA could be severed from the rest of 503A and that the remainder of 503A is valid and in force.

The Fifth Circuit's severability ruling conflicts with an earlier decision by the United States Court of Appeals for the Ninth Circuit, which held that the unconstitutional parts of section 503A are not severable and that all of section 503A is therefore void. *Western States Medical Center v. Shalala*, 238 F.3d 1090 (9th Cir. 2001). FDA has determined at this time that it will apply the non-advertising provisions of section 503A to entities covered by this provision that are located within the jurisdiction of the Fifth Circuit (i.e., Texas, Louisiana, and Mississippi) as well as to the plaintiffs that brought the *Medical Center Pharmacy* case. Elsewhere, including in Massachusetts, the agency will continue to follow the enforcement approach reflected in the Compliance Policy Guide (CPG) section 460.200 ["Pharmacy Compounding"] issued by FDA on May 29, 2002 (*see Notice of Availability*, 67 *Fed. Reg.* 39,409 (June 7, 2002)).

Your letter states that your firm does not introduce unapproved drugs into interstate commerce and does not need approved NDAs before dispensing its compounded medications. We disagree. As explained above, FDA regards compounded drugs as new drugs that require agency approval before they are introduced into interstate commerce. Your firm's compounded products lack this approval and therefore violate the FDCA.

Also as explained above, while compounded drugs violate the FDCA, FDA generally exercises enforcement discretion when they are the result of traditional pharmacy compounding. This discretion is contingent on factors such as the preparation of patient-specific drugs that meet medical needs for which FDA-approved drugs are unavailable.

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[1] In 1997, Congress enacted, as part of the Food and Drug Administration Modernization Act of 1997 (FDAMA), a provision that related to pharmacy compounding, codified in section 503A of the FDCA (21 U.S.C. § 353a).

You state that you compound topical anesthetic formulas solely in accordance with formulas determined by the prescribing physicians. We acknowledge that you will require physicians to specify the chemical formulation on each patient-specific prescription for compounded topical anesthetic drugs. You also asked us to advise you whether using the term "triple anesthetic cream" to describe your compounded drug product is problematic. We find that use of this term implies the standardization of a compounded drug product rather than extemporaneous compounding for individually identified patients.

In the Warning Letter, FDA also expressed concern that you were generating sales for the "triple anesthetic cream" by providing physicians with "courtesy prescriptions" (*i.e.*, free samples) of compounded drugs, without valid prescriptions that respond to patient-specific medical need, which would indicate the distribution by your firm of a standardized drug product. The development of a standardized drug product is inconsistent with the traditional practice of pharmacy compounding where pharmacists extemporaneously compound drugs upon receipt of valid prescriptions. In your response you assert that these "courtesy samples" are dispensed "only upon receipt of a valid prescription from a licensed practitioner to meet the unique medical needs of a particular patient" and that these are not samples as that term is defined in the Prescription Drug Marketing Act (PDMA). The Warning Letter did not allege that your practice violates the PDMA, and FDA does not take a position on this issue at this time. Nevertheless, we acknowledge your response that you provide a small amount of medication free of charge only upon receipt of a valid prescription. We will evaluate in a future inspection your current practices and any changes that you make to those practices and assess whether, despite these practices and changes, you produce standardized topical anesthetic products. We will not exercise enforcement discretion toward such products.

Please note that your letter does not alleviate our concern about the health risks associated with the topical anesthetics compounded by your firm. You state that "Virtually all drugs, including manufactured drugs, pose serious health risks if they are misused by physicians or patients." But the drugs compounded by your firm may be dangerous even if used as directed because they are extremely potent in comparison to FDA-approved topical anesthetic drugs. As noted in the Warning Letter, these risks are exacerbated if the safety-related information that accompanies these products is deficient.

We acknowledge that you have stated that you no longer dispense prescriptions for compounded products containing trypan blue or 20% aminolevulinic acid solution.

With regard to the repackaging of Avastin, we acknowledge your assertion that you repackage the product only upon receipt of a valid prescription from a licensed practitioner for an individual patient and your argument that this repackaging constitutes

the practice of pharmacy. However, each step in the manufacture and processing of a new drug, including packaging, must be approved by FDA, whether carried out by the original manufacturer or, in most cases, by a repackager. Pharmacists are not exempt from this requirement; however, FDA's Compliance Policy Guide on repackaging (Compliance Policy Guide Sec. 446.100, Regulatory Action Regarding Approved New Drugs and Antibiotic Drug Products Subjected to Additional Processing or other Manipulations) provides that the agency will exercise enforcement discretion toward pharmacists who repackage approved drugs within the practice of pharmacy for use consistent with the drug's approved labeling. Your repackaging is not consistent with Avastin's approved labeling, where you repackage the drug from vials into syringes, and where the labeled precautions include "discard any unused portion left in a vial...."

FDA is concerned about the manipulation of sterile products when a sterile container is opened or otherwise entered to conduct manipulations. The moment a sterile container is opened and manipulated, a quality standard (sterility) is destroyed and previous studies supporting the standard(s) are compromised and are no longer valid. We are especially concerned with the potential microbial contamination associated with splitting Avastin—a single-use, preservative-free vial—into multiple doses. When used intravitreally, microbes could cause endophthalmitis, which has a high probability for significant vision loss. The absence of controls over storage, and delays before use and after repackaging, only exacerbate these concerns.

As stated in the Warning Letter, your repackaging is not consistent with Avastin's approved labeling; therefore, for the reasons stated in the warning letter, we believe that your firm is distributing an unapproved new drug in violation of section 505 of the FDCA and a misbranded drug in violation of section 502(f)(1) of the FDCA.

Finally, we acknowledge your concern about the time between our last inspection of your pharmacy and the issuance of the Warning Letter. We agree that the length of intervening period was unusual. This in no way diminishes our serious concerns about your firm's operation.

Your firm must promptly correct the violations noted in the December 4, 2006, Warning Letter, and establish procedures to assure that such violations do not recur. Its failure to do so may result in enforcement action, including seizure of the firm's products and/or an injunction against the firm and its principals.

In a future inspection, we will confirm the commitments that you made in your response. We also will verify that your firm's compounding practices are consistent with the policy articulated in the CPG, and that your firm's operation is not otherwise at odds with the conditions under which the agency exercises enforcement discretion towards pharmacy compounding.

Please direct any questions you have to Bruce Ota, Compliance Officer. U.S. Food and Drug Administration, New England District Office, One Montvale Ave., 4th Floor, Stoneham, MA 02180.

Sincerely,

Bruce R. Ota
Compliance Officer
New England District Office

NWE: BRO/MSS

cc: R, CF, BRO, WL File

BEFORE THE STATE BOARD OF PHARMACY

STATE OF COLORADO

Case No. 2011-3973

CEASE AND DESIST ORDER

IN THE MATTER OF THE UNAUTHORIZED AND UNLAWFUL DISTRIBUTION OF PRESCRIPTION DRUGS AND/OR COMPOUNDED PRESCRIPTION DRUGS IN COLORADO BY NEW ENGLAND COMPOUNDING CENTER, INC.,

Respondent.

Pursuant to guidance established by the Colorado State Board of Pharmacy ("Board") at its January 15, 2009 meeting, documentation has been considered, including, but not limited to, the written complaint dated April 13, 2011, 2011, in the above-captioned matter.

Based upon this review, the Board hereby finds that it has jurisdiction over Respondent and the subject matter herein, and that there exists credible evidence that Respondent has acted without the required license or registration, in violation of §12-22-130(2) and 12-22-802, C.R.S.

The Board finds as follows:

1. Respondent's location at 697 Waverly St, Framington, MA 01702 is licensed or registered with the Board as a nonresident prescription drug outlet to dispense and deliver prescription drugs and/or compounded prescription drugs in the State of Colorado pursuant only to valid, patient-specific prescription orders.

2. Respondent's location at 697 Waverly St, Framington, MA 01702 is not licensed or registered to distribute stock prescription drugs and/or compounded prescription drugs in the State of Colorado.

3. On or around January 17, 2011 and March 24, 2011, Respondent distributed a stock compounded prescription drug from 697 Waverly St, Framington, MA 01702 to a prescription drug outlet in the State of Colorado.

4. Respondent's conduct constitutes the unlawful distribution of prescription drugs into the State of Colorado, in violation of §12-22-130(2) and 12-22-802, C.R.S.

WHEREFORE, pursuant to §12-22-125.2(9), C.R.S., the Board hereby ORDERS that Respondent immediately CEASE AND DESIST in engaging in the unlawful distribution of prescription drugs in the State of Colorado, in violation of §§12-22-130(2) and 12-22-802, C.R.S.

Within ten days after service of this order to cease and desist, Respondent may request a hearing on whether such acts or practices in violation Article 22 of Title 12, C.R.S. have occurred. Such hearing shall be conducted pursuant to §§24-4-104 and 24-4-105, C.R.S.

The Board authorized the undersigned representative to sign this Cease and Desist Order on its behalf.

DATED this 15th day of April 2011.

STATE BOARD OF PHARMACY

BY: Wendy Anderson

Wendy Anderson
Program Director
1560 Broadway, Suite 1300
Denver, Colorado 80202

[redacted]

From: Coffey, James D (DPH)
Sent: Friday, July 27, 2012 7:34 AM
To: Manning, Susan (DPH); Penta, Samuel J (DPH); [redacted]
Subject: FW: New England Compounding Center
Attachments: NECC.pdf

FYI for follow up discussion

JD

From: Coffey, James D (DPH)
Sent: Friday, July 27, 2012 7:33 AM
To: [redacted]
Subject: RE: New England Compounding Center

[redacted]

Please be advised that I am in receipt of the special report.

The Massachusetts Board of Pharmacy will respond as soon as possible following a thorough eview and analysis of the same.

If additional information is necessary, please contact me at [redacted]

Sincerely, JD

James D. Coffey
Director
Massachusetts Board of Registration in Pharmacy
Department of Public Health
Division of Health Professions Licensure
[redacted]

From: [redacted]@dora.state.co.us]
Sent: Thursday, July 26, 2012 3:06 PM
To: Coffey, James D (DPH)
Subject: New England Compounding Center

James

Attached is the Special Report submitted to the Chief Inspector for the Pharmacy Board in Colorado concerning the receipt of non-patient specific compounded products into Colorado. Included in this

report is the email correspondence with [redacted] with the FDA. Her direct phone number is [redacted] and her email is [redacted]

I would appreciate any information that the Massachusetts Board could provide concerning if this practice is allowed under Massachusetts pharmacy law.

Thank you.

[redacted]

[redacted]
Pharmacy Inspector
Colorado Department of
Regulatory Agencies
Division of Registrations
Board of Pharmacy
[redacted]
Consumer Protection

[redacted]

From: [redacted]@fda.hhs.gov>
Sent: Monday, July 16, 2012 2:54 PM
To: [redacted]
Cc: Wardwell, Amber; [redacted]
Subject: FW: New England Compounding Center (NECC)
Attachments: Attachment - 1.pdf; Attachment - 2.pdf; Attachment - 3.pdf; hppscan45.pdf

Hi [redacted]

I checked our Registration database and New England Compounding Center is not listed as having registered with us as a manufacturer. With this e-mail, I am copying our New England District Compliance staff with the information you provided (invoice for the injectable hyaluronidase to Delta County Memorial Hospital) along with the Cease and Desist documents [redacted] sent last year regarding NECC (see e-mail string below). I would suggest you get in touch with the Massachusetts Board of Pharmacy if you haven't already to inform them of the firm's activity and to see if there are any actions they may wish to take especially in light of your Cease and Desist Order.

I also checked the status of Wedgewood Pharmacy in New Jersey. They also are not listed in our database as having registered as a manufacturer. Under a separate e-mail, I will copy our New Jersey District Office with the invoice you collected, but as in the NECC case, you may wish to contact your counterparts with the New Jersey Board of Pharmacy.

Let me know if you have any questions or wish to discuss further.

[redacted]

From: Wardwell, Amber
Sent: Tuesday, May 10, 2011 3:07 PM
To: [redacted]
Subject: FW: New England Compounding Center (NECC)

Thanks [redacted]

[redacted] is the CO for NECC. I'll ask him to follow up if we have any questions.

Amber

From: [redacted]
Sent: Tuesday, May 10, 2011 4:19 PM
To: Wardwell, Amber; [redacted]
Subject: FW: New England Compounding Center (NECC)

Hi Amber and [redacted]

I had a phone call with [redacted] of the Colorado Board of Pharmacy regarding New England Compounding Center (NECC). Attached is the background information from Chris as well as the Cease and Desist Order that the Board issued to NECC regarding their illegal distribution of compounded drugs to hospitals in the Denver metropolitan area. The firm is neither registered or listed with the State to do business as a drug outlet. I know that you have some previous reg history with this firm and that they were the recipient of at least one warning letter. This is just FYI but if you have any questions, please feel to give me a call to discuss.

[redacted]

From: [redacted]@dora.state.co.us]
Sent: Tuesday, May 10, 2011 12:29 PM
To: [redacted]
Subject: New England Compounding Center (NECC)

HI [redacted]

Attachment – 1 is the report and exhibits that lead to the Cease and Desist Order;

Attachment – 2 is additional documents Pharmacy Board staff obtained at another facility (while related to NECC, it's unrelated to what actually led to the Cease and Desist Order); and

Attachment – 3 is the actual Cease and Desist Order.

As always, thanks for your help.

[redacted]

[redacted]
Chief Pharmacy Inspector
Colorado Department of
Regulatory Agencies
Division of Registrations
Board of Pharmacy
[redacted]

Consumer Protection

STATEMENT OF INTERIM COMMISSIONER DR. LAUREN SMITH ON NECC INVESTIGATION

BOSTON -- Tuesday, November 6, 2012 – The following is a statement from Massachusetts Department of Public Health (DPH) Interim Commissioner Dr. Lauren Smith:

Today I am announcing a development in our ongoing investigation into NECC and administrative changes at the Massachusetts Board of Pharmacy. These personnel actions stem from troubling information that has come to light during our ongoing review of the Board's oversight of NECC.

We have discovered a Colorado Board of Pharmacy complaint against NECC, which was forwarded to James D. Coffey, Director of the Massachusetts Board of Pharmacy, on July 26, 2012.

The information shared by Colorado showed that NECC had distributed manufactured drugs to many hospitals in that state between 2010 and 2012 without patient-specific prescriptions, in violation of NECC's Colorado and Massachusetts licenses. The Colorado Board of Pharmacy contacted the FDA with this information and the FDA confirmed to them that NECC was not a licensed manufacturer.

As seen in the attached documents, this information was provided in detail by Colorado to Mr. Coffey in July, which he then forwarded to Board attorney Susan Manning and Board inspectors. The director of the Board is responsible for ordering investigations. Mr. Coffey failed to order an investigation or take any other action on the Colorado complaint.

It is incomprehensible that staff did not act on the Colorado complaint given NECC's past, and their responsibility to investigate complaints. Following the outbreak, staff also failed to disclose the existence of Colorado's complaint to leadership at DPH.

As a result of these findings, we have terminated James Coffey and placed Susan Manning, a member of a bargaining unit, on administrative leave pending the final conclusions of our investigation. We have identified highly qualified individuals to fill these positions and the important work of the agency will continue with even greater resolve at this critical juncture.

There is no evidence at this time that staff informed Board of Pharmacy members about the Colorado issues. We continue to interview all Board members as part of

our investigation into their handling of this situation and will not hesitate to make further changes and personnel actions if we deem them to be necessary.

Since starting as interim commissioner, I have promised and delivered swift and decisive actions.

I find the actions of NECC reprehensible. We have the right to expect that all companies producing medication for use in delivering health care to comply with laws designed to protect patient safety. But I also expect the staff charged with overseeing these companies to perform their duties with the highest standards of quality and supervision. I believe that failed to happen here.

This investigation and the Department's thorough response will not stop until we have a complete understanding of what happened, assign accountability where it is warranted and can be certain the failures that led to this tragedy never happen again.

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FOR IMMEDIATE RELEASE:
November 7, 2012

FURTHER INFORMATION:
Anne Roach (617) 624-5006

STATEMENT OF INTERIM COMMISSIONER DR. LAUREN SMITH ON NECC INVESTIGATION

BOSTON -- Wednesday, November 07, 2012 – The following is a statement from Massachusetts Department of Public Health (DPH) Interim Commissioner Dr. Lauren Smith:

Today I am announcing a development in our ongoing investigation into NECC and administrative changes at the Massachusetts Board of Pharmacy. These personnel actions stem from troubling information that has come to light during our ongoing review of the Board's oversight of NECC.

We have discovered a Colorado Board of Pharmacy complaint against NECC, which was forwarded to James D. Coffey, Director of the Massachusetts Board of Pharma cy, on July 26, 2012.

The information shared by Colorado showed that NECC had distributed manufactured drugs to many hospitals in that state between 2010 and 2012 without patient -specific prescriptions, in violation of NECC's Colorado and Massachusetts l icenses. The Colorado Board of Pharmacy contacted the FDA who confirmed that NECC was not a licensed manufacturer.

As seen in the attached documents, this information was provided in detail by Colorado to Mr. Coffey in July, which he then forwarded to Boa rd attorney Susan Manning and Board inspectors. The director of the Board is responsible for ordering investigations. Mr. Coffey failed to order an investigation or take any other action on the Colorado complaint.

It is incomprehensible that Mr. Coffey and Ms. Manning did not act on the Colorado complaint given NECC's past, and their responsibility to investigate complaints. Following the outbreak, staff also failed to disclose the existence of Colorado's complaint to leadership at DPH.

As a result of these findings, we have terminated James Coffey and placed Susan Manning, a member of a bargaining unit, on administrative leave pending the final conclusions of our investigation. We have identified highly qualified individuals to fill these positions and the important work of the agency will continue with even greater resolve at this critical juncture.

There is no evidence at this time that staff informed Board members about the Colorado issues.

I find the actions of NECC reprehensible. We have the righ t to expect that all companies producing medication for use in delivering health care to comply with laws designed to protect patient safety. But I also expect the staff charged with oversight to perform their duties to the highest standards. That failed to happen here.

Since starting as interim commissioner, I have promised and delivered swift and decisive actions. This investigation and the Department's thorough response will not stop until we have a complete understanding of what happened, assign acco untability where it is warranted and can be certain the failures that led to this tragedy never happen again.

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[redacted]

From: Pontikas, Jean (DPH)
Sent: Tuesday, November 16, 2004 2:22 PM
To: Young, Charles (DPH)
Cc: Coffey, James D (DPH); Manning, Susan (DPH)
Subject: RE: NECC

Thank you for the update.

-----Original Message-----
From: Young, Charles (DPH)
Sent: Monday, November 15, 2004 1:07 PM
To: Pontikas, Jean (DPH)
Cc: Coffey, James D (DPH); Manning, Susan (DPH)
Subject: NECC

Hi Jean;

Wanted to update you on the above-referenced matter. The company (compunding pharmacy) did not accept the consent agreement the Board offered (probation + terms) and the counter offer submitted by his counsel will be discussed with the Board next Tuesday(11/23/04).

I will keep you updated

cy

Charles R. Young, R.Ph., Executive Director
Board of Registration in Pharmacy
Division of Health Professions Licensure
[redacted]
tel:
e-mail:
fax:
web:

[redacted]

From: Pontikas, Jean (DPH)
Sent: Friday, October 28, 2005 4:00 PM
To: Young, Charles (DPH)
Cc: Manning, Susan (DPH); Coffey, James D (DPH); Penta, Samuel J (DPH)
Subject: RE: Barry Cadden/NECC

Yes. HI Carol - please set up a meeting to discuss this and ask Chuck for names of others who should be invited. Thanks.

-----Original Message-----
From: Young, Charles (DPH)
Sent: Friday, October 28, 2005 2:04 PM
To: Pontikas, Jean (DPH)
Cc: Manning, Susan (DPH); Coffey, James D (DPH); Penta, Samuel J (DPH)
Subject: FW: Barry Cadden/NECC

Hi Jean:

Could Carol set up a time next week to discuss these cases?

Thanks

Chuck

Please Note Change in Contact Information
Charles R. Young, R.Ph., CFE
Executive Director
Board of Registration in Pharmacy
[redacted]

-----Original Message-----
From: [redacted]
Sent: Thursday, October 27, 2005 9:04 AM
To: Young, Charles (DPH)
Subject: Barry Cadden/NECC

Hi, Chuck-
When we last communicated about Barry Cadden/NECC, there was talk of having a meeting to sort out a way to proceed. Should we try to do that?
Thanks. [redacted]

[redacted]
Prosecuting Counsel
Department of Public Health
Office of General Counsel
[redacted]

[redacted]

From: Young, Charles (DPH) [redacted]
Sent: Friday, November 18, 2005 9:41 AM
To: [redacted]; Pontikas, Jean (DPH)
Cc: Manning, Susan (DPH)
Subject: RE: NECC/Cadden

A board-approved evaluator has been identified as: Pharmaceutical Systems, Inc. [redacted]

Please Note Change in Contact Information
Charles R. Young, R.Ph., CFE
Executive Director
Board of Registration in Pharmacy
[redacted]

-----Original Message-----
From: [redacted]@state.ma.us]
Sent: Friday, November 18, 2005 9:41 AM
To: Pontikas, Jean (DPH); Young, Charles (DPH)
Cc: Manning, Susan (DPH)
Subject: RE: NECC/Cadden

-----Original Message-----
From: Pontikas, Jean (DPH)
Sent: Friday, November 18, 2005 9:32 AM
To: Young, Charles (DPH)
Cc: Manning, Susan (DPH); [redacted]
Subject: RE: NECC/Cadden

Yes - it looks like she left it blank for that name - Please confer with her and resolve who is communicating with NECC about that/this. Thanks.

-----Original Message-----
From: Young, Charles (DPH) [redacted]
Sent: Friday, November 18, 2005 9:23 AM
To: Pontikas, Jean (DPH)
Subject: RE: NECC/Cadden

I already provided comments and I think it looks fine

I let her know as well(although I thought we were going to include the actual name of the outside "evaluator" in the agreement)

322.2 (3)(a)

Please Note Change in Contact Information
Charles R. Young, R.Ph., CFE
Executive Director
Board of Registration in Pharmacy
[redacted]

-----Original Message-----
From: Pontikas, Jean (DPH) [redacted]
Sent: Friday, November 18, 2005 9:07 AM
To: [redacted]; Young, Charles (DPH)
Cc: Manning, Susan (DPH)
Subject: RE: NECC/Cadden

I think it looks fine and don't have any comments to offer. Chuck?

-----Original Message-----
From: [redacted]
Sent: Friday, November 18, 2005 8:52 AM
To: Pontikas, Jean (DPH); Young, Charles (DPH)
Cc: Manning, Susan (DPH)
Subject: NECC/Cadden

[redacted]
Prosecuting Counsel
Department of Public Health
Office of General Counsel
[redacted]

[redacted]

From: Pontikas, Jean (DPH)
Sent: Friday, December 02, 2005 2:33 PM
To: Coffey, James D (DPH); Young, Charles (DPH)
Subject: FW: NECC/Cadden; phone number for Pharmaceutical Systems

Perhaps some more good news.

-----Original Message-----
From: [redacted]@state.ma.us]
Sent: Friday, December 02, 2005 2:29 PM
To: Young, Charles (DPH)
Cc: Pontikas, Jean (DPH); Manning, Susan (DPH)
Subject: NECC/Cadden; phone number for Pharmaceutical Systems

I spoke with [redacted] NECC/Barry Cadden's attorney, today. They are interested in the Consent Agreement and [redacted] would like to identify an evaluator for Board approval. He mentioned [redacted] who has worked with NECC, and I said that the Board was interested in a new evaluator, so there would be absolutely no question about independence. I provided him with the name, address and phone number of [redacted] as one evaluator that has been approved by the Board. He expressed some preference for an in-state evaluator, because of the additional cost which may be involved in transportation and housing for an out-of-state evaluator. He agreed that he will work on this issue and be back in touch next week.

[redacted]
Prosecuting Counsel
Department of Public Health
Office of General Counsel
[redacted]

[redacted]

From: Penta, Samuel J (DPH)
Sent: Monday, December 19, 2005 9:13 AM
To: [redacted]
Subject: FW: NE Pharm

-----Original Message-----
From: Penta, Samuel J (DPH)
Sent: Friday, September 16, 2005 8:47 AM
To: [redacted]
Subject: FW: NE Pharm

-----Original Message-----
From: Young, Charles (DPH)
Sent: Friday, September 16, 2005 8:23 AM
To: [redacted]
Cc: Coffey, James D (DPH); [redacted]
Subject: RE: NE Pharm

Good Morning [redacted]

Please be advised that at the present time the Board of Registration in Pharmacy does not have any such 5% rule and I suspect that the registrant is well aware that the only way he is permitted to provide a legend drug product is pursuant to a written or oral prescription.

I really appreciate this alert and will forward it through appropriate channels to ensure the registrant is made aware of this fact.

Sincerley,

Chuck Young

Please Note Change in Contact Information
Charles R. Young, R.Ph., CFE
Executive Director
Board of Registration in Pharmacy
[redacted]

-----Original Message-----
From: [redacted]
Sent: Friday, September 16, 2005 9:09 AM
To: Young, Charles (REG)
Subject: RE: NE Pharm

Chuck,

We have looking to purchase some products from New England Compounding Center in Framingham. The products we are looking at are not available from pharmaceutical manufacturers or have been backordered by pharmaceutical

manufacturers.

Our business with them as been on a per patient prescription basis. They are willing to sell us items without a patient name and dispense the prescription to Brigham and Women's Hospital as long as the products are used in-house. They claim that they are
allowed to do this without a patient name as long as this type of prescription volume is less than 5% of there total prescription filling.

Does this sound ok? They claim that they have been in contact with the Board of Pharmacy regarding this issue.

Thanks [redacted] .

Pontikas, Jean (DPH)

From: Manning, Susan (DPH)
Sent: Monday, April 24, 2006 2:12 PM
To: Pontikas, Jean (DPH)
Cc: Young, Charles (DPH); Coffey, James D (DPH)
Subject: NECC Follow-Up

Attachments: 2 guilty of selling bad sterilizers to hospitals Chicago Tribune.html


2 guilty of selling bad steril...

i Jean - Note conclusion as reported in 4/14/06 news item.

On Chuck's return today, we reviewed the NECC communication dated 4/19/06 (I believe a copy was placed in your box last week). The very specific (tho not clearly major) items to be completed at this point appear to be recommended HVAC work scheduled for May 10; gowns and sleeves ordered are expected to be received this week; and new procedures re: sterilizing filter testing to commence with next lot ordered form Millipore (projected date not specified in response).

The NECC response comments re: Par. 2. re: one way flow in Clean Room 2 (not agreed to be "wise" by NECC - causing possibility of outside air flowing into clean room from continuous egress thru emergency exit) and re: Par. 3. re: retention of certain non-essential equipment in current location appears to not clearly present a risk to sterility since sterile prep is performed in the microenvironments in this room which is maintained as a clean room. These last items can be reviewed by the Board at the 5/9 meeting.

Let us know if you have any questions or direction - SM

2 guilty of selling bad sterilizers to hospitals

By Michael Higgins
Tribune staff reporter
Published April 14, 2006

A federal jury found two medical-products executives guilty Thursday of charges that they sold millions of dollars in faulty sterilization equipment to hospitals in the 1990s.

Ross Caputo, former CEO of Mundelein-based Abtox Inc., and Robert Riley, the company's former vice president of regulatory affairs, falsely represented to hospitals that the U.S. Food and Drug Administration had approved their sterilization machines, prosecutors said.

The FDA had warned Abtox that the machines should not be sold, and the product's inability to properly sterilize medical instruments caused 18 patients to be blinded in one eye, prosecutors said.

Abtox sold 168 of the machines from about 1994 to 1998, earning about $18 million in revenue, prosecutors said. Abtox later went bankrupt.

Caputo slumped back in his chair as a courtroom deputy read the jury's verdict. Riley dropped his head, covering his face with his arms.

Both Caputo and Riley were convicted on more than a dozen charges, including conspiracy to defraud the FDA and sale of a misbranded medical device.

The trial took nine weeks. The jury returned its verdict in less than two days.

U.S. District Judge Ruben Castillo is scheduled to sentence both men on July 12. Under federal guidelines, they could face 10 years or more in prison, prosecutors said.

Riley's attorney Jonathan Feld said he expects his client to appeal, but he declined to comment further. An attorney for Caputo could not be reached.

The product at issue uses chemicals to sterilize medical instruments at low temperatures. Caputo and Riley said they had acted in good faith and believed they had the right to market the product.

But Assistant U.S. Atty. Michael Gurland argued that the FDA had approved a smaller version of the Abtox sterilizer for certain purposes.

That product wouldn't sell, so Abtox, which was struggling financially, created a far larger, unapproved product and marketed it aggressively to hospitals, Gurland said.

"The defendants pulled a bait-and-switch on the FDA," Gurland said Thursday. He said that during the trial, an Abtox official testified that Caputo told him to sell as many of the sterilizers as he could "before the FDA catches on."

The injured people included three patients at Ravenswood Hospital in 1996, Gurland said.

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mjhiggins@tribune.com