Interim Clinical Guidance during the Multistate Fungal Meningitis Outbreak Investigation

Moderator: Leticia R. Davila

Presenters: Melissa K. Schaefer, MD, Tom Chiller, MD, MPH, and Janet Woodcock, MD
Q&A: Matthew Wise, PhD
Date/Time: October 25, 2012 2:00 pm ET

NOTE: This transcript has not been reviewed by the presenter and is made available solely for your convenience. A final version of the transcript will be posted as soon as the presenter's review is complete. If you have any questions concerning this transcript please send an email to coca@cdc.gov.

Coordinator:

Welcome and thank you for standing by. At this time all participants are in listen only mode. After the presentation we will conduct a question and answer session. Today's conference is being recorded. If you have any objections you may disconnect at this time. And now I'd like to introduce your host for today's conference, Leticia Davila. You may begin.

Leticia Davila:

Thank you (Jeff). Good afternoon, I am Leticia Davila and I am representing the Clinician Outreach and Communication Activity, COCA, with the Emergency Communication System at the Centers for Disease Control and Prevention. I am delighted to welcome you to today's COCA conference call, *Interim Clinical Guidance During the Multi-State Fungal Meningitis Outbreak Investigation*. We are pleased to have with us today, Doctor Schaefer and Doctor Chiller, from the Centers for Disease Control and Prevention, Doctor Janet Woodcock from the Food and Drug Administration. They will provide updates to the current epidemiology of the outbreak and discuss CDC's recommended treatment guidance and rationale. There are no continuing education or slides provided for this call. Event-specific resources for clinicians are available on our COCA Website at emergency.cdc.gov/coca.

Our first presenter today is Doctor Melissa Schaefer. Doctor Schaefer is a Medical Officer in the Division of Healthcare Quality Promotion at the CDC. She currently works on the Ambulatory and Long-Term Care Team in the division. Her efforts focus on infection prevention in ambulatory care settings, with a particular emphasis on ambulatory surgical centers and issues related to injection safety.

Our second presenter is Doctor Tom M. Chiller. Doctor Chiller serves as the Deputy Chief of the Mycotic Diseases Branch. He is board certified and is a faculty member in the Division of Infectious Diseases at the Emory School of Medicine. He practices infectious diseases at the Veterans Affairs Hospital in

Atlanta. He has authored numerous articles and book chapters and given many lectures on public health surveillance and infectious diseases.

Our final presenter today is Doctor Janet Woodcock. Doctor Woodcock is a Director of the Center for Drug Evaluation and Research at the Food and Drug Administration.

In addition to today's presenters, Doctor Matthew Wise, an Epidemiologist in CDC's Division Healthcare Quality Promotion will be available to answer questions during the Q and A section of today's COCA call.

At the end of the presentation, you will have the opportunity to ask the presenters questions. On the phone dialing star 1 will put you in the queue for questions. Questions will be limited to clinicians who would like information on clinical guidance related to the multi-state fungal meningitis outbreak investigation. For those who have media questions, please contact CDC Media Relations at 404-639-3286 or send an email to media@cdc.gov. At this time please welcome our first presenter, Doctor Schaefer.

Melissa Schaefer:
Thanks Leticia. As Leticia mentioned, I'm going to give a very brief overview of the outbreak, give you the update case counts for the day. And then I'll turn it over to Doctor Chiller who is going to update on the clinical updates related to this outbreak, including some recently posted guidance.

And then finally we'll turn it over to Doctor Woodcock who will also give a brief update on FDA actions and activities for you all. And then we'll spend the majority of the time answering any questions that you might have.

So as, you know, as we said on the prior COCA call, CDC in collaboration with the state and local health departments and FDA are investigating a multi-state outbreak of fungal infection among patients who have received contaminated steroid product from a single compounding pharmacy, the New England Compounding Center.

Several patients have suffered strokes that are believed to have resulted from their meningitis infection. And we've also identified fungal infections associated with peripheral joints, like the knee, shoulder or ankle.

All the information about the outbreak, the updated guidance are on the CDC Website. As we've said before, we encourage you to check their daily or multiple times a day because we do take great pains to keep that updated with the most up to date information.

So make sure that you're checking back and looking at the date stamps on the documents that you're working with to make sure that you have the most up to date information.

I now just want to give a quick update on the case count for today. And then I'm going to turn it over to Doctor Chiller to go over some clinical updates.

As of today, Thursday, October 25, our current case count is 328, including 24 deaths being reported from 18 states. That information and the state count by state will be posted on the CDC Website. So you can check there to look at the individual state level information. And with that I'll turn it over to Doctor Chiller.

Tom Chiller:
Thanks Doctor Schaefer. It's a pleasure to be here again on a COCA call to talk about this fungal meningitis outbreak. I want to point out that from the case counts that Doctor Schaefer gave, we still have I think only five joint infections included in that case count. And so we still are not seeing very many joint infections. And we want to encourage physicians that if they do have patients that have had injections in joints where they are concerned about a possible infection, that they do do, you know, a vigorous work up to try and diagnose infection. And report that to your state health and local health departments so that we can hear more about these infections, if indeed they are occurring.

So I'm not going to spend a lot of time detailing our treatment recommendations. We have posted them on our website. As you heard from Doctor Schaefer, we take great pains to post recommendations as soon as we make changes to them. And I can assure you that with our clinical expert team, we are reviewing these guidelines on a daily basis. And modifying them based on information we receive from treating clinicians as well as case reports of patients with these infections.

So I want to emphasize a couple things. One is that it's important to note that negative fungal culture or a negative fungal polymerase chain reaction, or PCR as you've heard referred to this test.

From a diagnostic specimen does not mean that the patient does not have a fungal infection. These tests are very insensitive unfortunately. And although have been helpful in helping us identify the primary fungus, which as you've heard is *Exserohilum*, a black brown mold.

They are not perfect in their ability to identify everyone with infection. And so it's important that if patients who have symptoms consistent with meningitis or joint infection and still don’t have positive cultures or

PCRs. They still can be cases. And indeed we expect that the majority of patients in this outbreak will actually unfortunately not have positive cultures or PCR tests.

We continue to recommend Voriconazole as our empiric antifungal therapy. We want to encourage that when giving Voriconazole, it is critically important to monitor blood levels. And we want those blood levels to be between 2 and 5.

We want you to get a blood level after five days of treatment. And then continue to get blood levels probably weekly for the first four to six weeks. You will - this will help maintain adequate levels and when levels are above 5, may help you adjust for any toxicities that you might be seeing.

I think the main thing that I want to highlight in the next couple of minutes is new guidance that we have posted on the management of asymptomatic patients who received epidural or paraspinal injections.

We used additional data from cohorts of case patients that we've received to date. And when analyzing this data, it indicates that patients who received epidural or paraspinal injections with a contaminated stored product within the last six weeks or 42 days may be at greatest risk for developing meningitis.

And therefore, we want clinicians to consider more additional and careful monitoring of these individuals.

The information we provided in the update on the Web gives some of this additional guidance to clinicians. And I'm going to briefly read some of that.

CDC's recommendations; however, on using antifungal therapy in a prophylactic fashion remains unchanged. And we do not advocate treating asymptomatic patients that do not have evidence of fungal meningitis by cerebral spinal fluid examination.

However, for patients who have received an epidural or paraspinal injection with one of the contaminated products within the last six weeks, we want to offer a couple different options for management.

One, you continue to closely monitor these patients for the development of symptoms with a low threshold to obtaining CSF should the patient become symptomatic.

And when you do a diagnostic lumbar puncture or other procedure to obtain CSF, they should be done preferably through a different site than where the epidural injection was given.

The other option which we estimated would reduce the maximal risk of stroke or death from approximately .4% to .3% in comparison to the first option that I just said, may also be considered.

In this scenario, one would obtain CSF or perform lumbar puncture, again preferably through a site where the epidural injection wasn't given. And if the cerebral spinal fluid examination showed less than or equal to 5 white blood cells, the patient would be continued to follow closely for onset of symptoms.

And if the patient remained asymptomatic, we would consider repeating weekly lumbar punctures or obtaining CSF weekly until the sixth week or 42-day period had passed since the last epidural or paraspinal injection with contaminated steroid product was given.

At which time the patient could continue to be monitored closely for the development of symptoms, again with a low threshold to obtain CSF.

Patients however, with greater than five white cells in CSF would be treated for fungal meningitis according to our current treatment guidelines.

So in making management decisions, clinicians should also consider the risk associated with obtaining CSF using lumbar puncture. Like post-lumbar puncture headaches, CSF leak, theoretical risk that fungi could be transferred from the epidural space into the subarachnoid space of a patient who has received these injections and then had a lumbar puncture.

I think it's important to note that in all of this modeling and in these high-risk patients, we know that the farther out you are from receiving an injection, the lower your risk becomes for developing meningitis or other infections. And so we want to emphasize that.

I think with that I will stop. And I will again, please refer you to our Website where this updated guidance and rational for all of our treatment guidance and diagnosis is outlined in detail.

And please, as Doctor Schaefer said, check back often as we are updating these on a very frequent basis. Thank you, Doctor Woodcock?

Janet Woodcock:

Hello, this is Janet Woodcock. Thanks for the opportunity to talk to everyone. On Monday we posted on our Website two NECC customer shipping lists. That where products were shipped on or after May 21, 2012.

And the first list includes - we have two lists. First is customer names and addresses organized by state. And this is per company, all right. The second list contains that information but is organized alphabetically by customer name.

And also includes specific products that they recorded that they shipped, the quantities of product shipped and the shipping date.

We did this to enable NECC customers involved in the recall and people who are communicating with patient to focus their attention on the products that were shipped during this time period, which are believed to be at the greatest risk of contamination.

And May 21, 2012 of course is the date the first of the three lots of methylprednisolone acetate implicated in the current outbreak was produced.

The list was prepared by FDA based on a list that was provided by NECC, after posting the list we found some technical problems with the posting that occurred when we extracted that information from the full list.

We reviewed, corrected and reposted those lists. And they are current. They are correct as far as what NECC records go. But be aware, we can't vouch for the completeness of the list provided by NECC.

Products shipped from them may be missing from the list. And the facility information may be incomplete. And we have heard from some hospitals and healthcare facilities that they believe they were listed in error.

However, this is what the firm had, their records of what they shipped and to whom it shipped. Nevertheless, this is the best list we have available to help inform facilities and providers of NECC products that were possibly shipped to their facility since May 21, 2012.

And we regard it more or less as a prompt for people as they go back and look at these products.

Of course we're asking people to isolate these products and recall - return them when possible. We recognize that the recall that’s being run by NECC has been problematic, difficult to contact them.

So it's most important for our point of view that these products remain quarantined at the site until you're able to send them back.

Now we've received a lot of questions about a related facility, Ameridose. Ameridose is another facility in Massachusetts compounding pharmacy that has common ownership with NECC.

FDA and the Massachusetts Board of Pharmacy are also inspecting this firm. Ameridose is also registered with FDA's as a manufacturer and repackager. And is licensed by the Mass Board of Pharmacy. And they have a much larger distribution of products then did NECC.

Ameridose entered into a voluntary agreement with the Massachusetts Board of Pharmacy to cease all pharmacy and manufacturing operations until November 5, 2012.

We have not implicated a recall of any Ameridose products at this time. When we do or if, not when, but if that were to occur then we would certainly notify the healthcare community immediately.

We are aware that many hospitals and clinics across the country are customers of Ameridose. And that the current production shutdown may impact supplies of certain drugs for certain healthcare systems and drugs that are in near shortage status.

We are - we have to make sure that the drugs in the drug supply are safe. But of course we also have a shortage program. And we try to make sure that needed drugs are available.

So we are working with those dual goals. If you're experiencing shortages, please refer to FDA's drug shortage Website for information on availability of drugs currently in shortage.

And if you believe there is a drug entering shortage, or you're experiencing that, please notify our drug shortage team at drugshortages@fda.hhs.gov. And they will get on the case and try to arrange for supplies to be made available.

Now we continue to receive reports from patients and healthcare providers of adverse affects from medications that were shipped by NEC. And, you know, obviously other drug manufacturers.

We are evaluating these reports for any link to NECC products. And we'll immediately notify the public if we identify any additional products that are linked to human disease at this point.

And we are also asking as people report these, especially say you're having clusters that they also talk to their state health department so that everybody is aware of the concerns.

We're asking clinicians and patients to report any suspected adverse events following the use of any of these products or products that are suspected to be NECC products to FDA's med watch program at 1-800-332-1088, or www.fda.gov/medwatch.

We have information about the outbreak on our Website. And the public may contact our Division of Drug Information. And that number is also available. And we are continuing to receive a fair amount of calls from the public about the outbreak.

And we have pharmacists available to provide information to the public. So I'll close with that and await questions. Thank you.

Leticia Davila:
Thank you Doctor Schaefer, Doctor Chiller and Doctor Woodcock for providing COCA audience with such a wealth of information.

As a reminder, Doctor Matthew Wise from CDC is available to answer any questions you may have.

We will now open up the lines for the question and answer session. Please remember that questions are limited to clinicians who would like information on clinical guidance related to the multi-state fungal meningitis outbreak investigation.

For those who have media questions, please contact CDC Media Relations at 404-639-3286 or send an email to media@cdc.gov. Thank you.

Coordinator:
If you would like to ask a question, please press star 1. Please un-mute your phone and record your name clearly when prompted. Your name is required to introduce your question.

To withdraw your question, please press star 2. Again if you would like to ask a question, please press star 1, one moment please for the first question. First question is from (Patricia Triplet). Your line is open.

(Patricia Triplet):
I am under treating one of our cases. And he is a 44-year-old gentleman who did not have an advance case, but an early case. He is taking Voriconazole and is having extreme fatigue. And that's his biggest symptom.

I've checked labs. I've done everything to try to figure out why. Is anyone else seeing extreme fatigue associated with these high doses of Voriconazole?

Tom Chiller:
Thank you for that question. This is Tom Chiller. No, you know, I have not heard reported extreme fatigue. We have heard of a lot of other affects from Voriconazole.

Most of them, as you could imagine, are CNS related. So visually related, visual hallucinations. We hearing some people are having word searching. So they're searching for words. They're - I wouldn't call them confused. But they're slightly sort of having inability to find the right word to respond to things.

And we have heard of some patients developing liver function abnormalities. Meaning their LFTs are slightly rising. I think that the CNS toxicities, and if the fatigue is something that is happening because of the CNS toxicity, these are completely reversible.

And perhaps, I'm not sure if you were able to get a Voriconazole level on this patient. But perhaps their level is slightly high. But no, we have not heard about fatigue yet being associated with Voriconazole.

Coordinator:
The next question is from Doctor (Florence). Your line is open.

Doctor (Florence):
Yes. I'd like to know what's the instance of a false positive? Having more than five white blood cells in a lumbar puncture? I'm just curious because we have asymptomatic patients. And they're already now most patients are four or five weeks out. What's going to be a false positive rate?

Tom Chiller:
Yes thanks for that question. That's a great question. And you're right. There will be a certain number of false positives so to speak, or patients that have a few white cells in their CSFs.

We know it will be extremely low. But we're not - we don’t have a good estimate of what that will be. But I think again, being overly cautious, which is what our recommendations are and sort of generating the worse case scenario.

That's why we've recommended this sort of six-week period. Although we know the risk will continue. But it will reduce even beyond that period. But over an abundance of caution, we're just recommending that

asymptomatics who are in this early period could potentially get serial lumbar punctures in order to assess their CSF.

I think that if you had a CSF that had greater than five white cells that you would clinically consider treating that patient empirically, although I do understand your worry about potentially over treating.

We think that over treating in this case will be very, very, very minimal. So we don't expect to see a lot of abnormal CSFs that are not linked to some process.

Doctor (Florence):
Can I ask you? Can I just ask a follow up? Two questions, but would you have a number of the false positives like in a regular - never mind this outbreak. Just let's say regular patients being tested.

Would you be aware of that, like that number of false positives elevated white counts in let's say a control patient population? One and two, do you think the number changes when you're from four to six weeks as most patients are from the four to six week period now?

Tom Chiller:
Yes so I mean these are great questions. And I don't have definitive answers for you because you can imagine that there just haven't been studies looking at a lot of normal, healthy people and doing lumbar punctures on them.

I can tell you from our experience with this outbreak, because there have been clinicians probably like many of you out there doing lumbar punctures on people that even are symptomatic coming in.

We know that even the majority of people with a mild symptom for example still are having negative lumbar punctures. So in my mind that would suggest that even those people where we would definitely be concerned about a positive lumbar puncture, we're seeing normal CSFs.

So at least it suggests that that number of false positives is going to be extremely low. I think in the risk calculations that we did and talking to our expert panel, we estimated it might be somewhere around 1% or less.

But again, I think that's probably an overestimation because as we're - when we're trying to understand and calculate risk, we try to overestimate some of those in order that we project the maximum risk for patients in these particular groups.

Doctor (Florence):
Okay thank you all for your help very much by the way.

Tom Chiller:
Thank you for your questions.

Coordinator:
(Theresa Devor) your line is open.

(Theresa Devor):
Thank you. At our surgery center we are using drugs from the NECC. But not the drugs causing the meningitis or the ones that's causing the problem.

But we're still having patients call with concerns. What do we need to tell them if they received drugs from the NECC?

Janet Woodcock:
This is Janet Woodcock from the FDA. What we have advised clinicians is than any drug that was put into a - from NECC that was shipped after May 21, 2012. We would like some follow up on those patients.

We have no assurance of sterility of any of those products. We do not though have any definitive cases of human disease from other products. But we would ask you to check with the patients and make sure that they don't have signs of infection, you know, particularly related to what they would get if they were administered a non-sterile NECC product at the site for example where they had their surgery.

So we are asking this not for every medication, but any medication that was an injectable product including an ophthalmic drug that was injected. Or used in conjunction with eye surgery, cardioplegic solutions and similar solutions that are, you know, exposed internally to the body and our intent should be sterile.

So we have asked that clinicians look back at all their patients since then who were exposed to NECC products.

Melissa Schaefer:
And this is Doctor Schaefer. I just wanted to tail on to what Janet was saying and make sure a point of clarification. It sounded like you said you're still using products from NECC? We just want to emphasize

that all NECC products have been recalled. You should not, nobody should be using any products from NECC currently.

(Theresa Devor):
No we're not.

Melissa Schaefer:
Okay, just wanted to make sure that was the case. Thank you.

(Theresa Devor):
Some patients are still calling, you know, with, you know, symptoms. Not really having signs of infections. But I think it's more we're getting calls, you know, of concern.

Janet Woodcock:
Certainly. And we had - we have a draft letter, this is Janet Woodcock from FDA again, on our Web page that we have drafted that you might consider sending out to your patients. We would expect they would call and be concerned if people have, of course, many illnesses. But we would ask them to be screened basically for infections that might have been related to the kind of administration of an NEC drug that they got.

(Theresa Devor):
Okay. Thank you very much.

Coordinator:
(Joanne Campbell) your line is open.

(Joanne Campbell):
Hi, we were just wondering was there any incident for retinal injections? Did anybody have any signs or symptoms from that?

Tom Chiller:
So this is Tom Chiller from CDC. And Doctor Woodcock can comment as well. But as Doctor Woodcock has been saying, to date we don’t have any firm evidence of any infections with any products from NECC, not associated with the three lots of MPA that we're currently reporting.

(Joanne Campbell):
Okay thank you.

Janet Woodcock:
That's correct. And we do not have any report - firm - confirmed reports of any, you know, eye infections that have been reported to us. And we're casting quite a wide net.

Tom Chiller:
Yes and however, as Doctor Woodcock mentioned, you know, we clearly want clinicians to follow up with patients that might have received the products that she has just outlined to find out how - if they are having any potential symptoms.

And I think that's what the FDA, the med watch report and information has been saying.

(Joanne Campbell):
Okay thank you.

Coordinator:
(Alexander Stemmer) your line is open.

(Alexander Stemmer):
Oh thank you so much. We have literally thousands of patients who have received either generic Furosemide or the generic forms of Toradol intravenously, or Reglan. And I wonder if any of those batches that have been sequestered have been cultured? And if so, do we have results? Doctor Chiller has indicated that culture may be insensitive. Is it insensitive to the zero level? Or should any of these batches be - should we be culturing any of these batches?

Janet Woodcock:
This is Janet Woodcock. We have cultured a number of samples of products from NECC during this period of concern. When we have definitive information on any of them, we will alert the public.

However, I think you have to realize that tens of thousands of units were shipped. And so, you know, us doing random cultures or other cultures may not really give us much information about the assurance of sterility.

We're basing our concerns on the sterility of these products based on what we found in the inspection and what we know about the facility.

So we don't - we aren't recommending one way or another that people culture their own - perform their own cultures. However, we will notify everyone if we have positive cultures from other products.

But the scope of the number of products means that we're not going to be able to do statistically valid sample to provide a lot of assurance.

Tom Chiller:
Yes and this is Doctor Chiller. And I just want to echo Doctor Woodcock's comments. And also talk, just you mentioned briefly about the sensitivity of culture. I was specifically referring to patient specimens.

I think FDA and their abilities to examine sterile products and un-sterile products for bacterial, fungal, other types of contaminants, they are very well versed in these methods.

And it's really important for, you know, for laboratories who know how to do this kind of testing to perform it. And I would be concerned if there were lots of individuals testing products, you know, without going through FDA or their local health or - and regulatory authority.

So I would encourage you to not do testing. And to let FDA continue to do the testing they're doing. And as Doctor Woodcock said, they will be reporting things out as soon as they find any issues or problems.

(Alexander Stemmer):
Thank you very much.

Coordinator:
(Jack) your line is open.

(Jack):
My question is we do epidural steroids on a lot of our patients. Now we sent out the letters as advised. We did not give any of the Solu-Medrol or the Kenalog.

However, we did give NECC medications. A lot of our patients routinely have migraines and chronic pain. So they already have signs that go along with the meningitis.

Our patients are calling. How should we advise them? Should we advise them to go get a lumbar puncture or?

Tom Chiller:

So are you talking about, just for clarification, are you talking about patients that received epidural injections with one of the three contaminated lots of MPA product?

(Jack):
No. They're not the contaminated lots. Ours were the betamethasone, which haven't been contaminated yet. But they have been recalled. When we sent out the letters, all of our patients are calling and having questions. And we can answer most of them.

But the ones that have symptoms and say that, you know, they match everything that goes with meningitis, but we can't rule it out because they migraines, they have all these other symptoms on a daily basis.

How should we advise them? Should we send them to the ER for lumbar puncture? Or just...

Tom Chiller:
Yes these are challenging cases. I think we need to be vigilant and we do need to be concerned if there are changes in their symptoms or if there are worsening in their symptoms.

Clearly you're right. Many of these patients have chronic pain. And we're hearing that from many of you out there who have been treating them. But I think what is helpful at least in the, and I can only speak again to confirmed cases that we have with the three lots of the MPA product.

Is that these patients have slightly different symptoms, worsening symptoms or symptoms that don't improve when they normally would. So you're absolutely right. You need to assess what is their baseline level of symptomatology. And how that might change.

But I think if you are concerned or uncomfortable with what they're telling you, then I think you do need to consider further diagnostic workup.

(Jack):
Thank you very much.

Coordinator:
(Clyde Goody) your line is open.

(Clyde Goody):

Yes my question is similar to the question that was asked just now. But I'm just wondering, is there any new information about the triamcinolone from NECC?

There was a suspected case. So far it did not grow any fungal - fungus in the culture. Is there any new information related to the triamcinolone product?

Janet Woodcock:
This is Janet Woodcock from the FDA. We have multiple triamcinolone lots under culture. Again, not a statistically representative sample what was out there. But we do have multiple lots under culture. And we will announce as early as possible if we find anything.

That doesn't rule out though that there could have been contamination based on, as I said, the conditions that we found.

(Clyde Goody):
Thank you.

Coordinator:
(Ellen Oaken) your line is open. (Katie Elvino) your line is open.

(Katie Elvino):
Hi, we're an eye facility. And my question is we use the dilating drops from NECC, like an hour before surgery. So we're trying to figure out is that - did you say in conjunction with surgery? I'm trying to find would dilating drops be in conjunction with surgery because (unintelligible), you know, know in the pre-op area, before the OR.

Janet Woodcock:
Yes well we could consider that in conjunction with surgery because then there was a wound. And if you had contamination, then it would likely remain.

(Katie Elvino):
Right but after the drop they would just - we would prep with Betadine. So it still would be a potential risk? Because it wasn't done in the OR.

Janet Woodcock:
Yes we're asking people to use their clinical judgment, all right, on these things because, you know, we can't, we don't know the circumstances in which all these were used. It's very difficult.

(Katie Elvino):
Yes of course. Just my doctors are concerns about, you know, alarming other patients if it's a low risk. Should they or shouldn't they contact them? I'm just trying to figure out if your ideas of conduct with surgery meant. And I know, I guess it's a gray area. I'm not sure.

Janet Woodcock:
It's a gray area. I think that's the answer.

(Katie Elvino):
Okay all right, thank you.

Janet Woodcock:
Thank you.

Coordinator:
(Greg Rally) your line is open.

(Greg Rally):
Yes I had a couple questions. One I believe Doctor Woodcock may have addressed. There was a draft letter. And I went on the Website. And I haven't been able to locate that.

And the second part of this was we are in the - formulating a list of patients that each of our physicians had that utilized the product. And my question is is it up to that physician then or the surgeon to go ahead and contact the patients? I just want to know where the ambulatory center's responsibility lies.

Janet Woodcock:
This is Janet Woodcock. You know, this - we are asking clinicians and facilities to do this. We don't have authority over, you know, this isn't a, you know, requirement.

We are asking or suggesting or urging that this be done to - for patient safety reasons. So I think that the clinicians involved in the ambulatory centers involved should get together and decide how they're going to address this issue.

But there's no, you know, requirement that the FDA is putting on any party to do this follow up.

(Greg Rally):

And the draft letter you spoke of Doctor? '

Janet Woodcock:
We're looking. It's on our meningitis page. We're looking at finding the URL and then we'll let you know when we have it here.

(Greg Rally):
Okay.

Janet Woodcock:
Well we can move on to another question maybe and I'll let you know when I find it.

Coordinator:
(Sidestreet Surgery Center) your line is open.

Woman:
This is for Doctor Woodcock please. We of course had all three contaminated lots in our surgery center. And we've contacted all of our patients. There have been multiple questions regarding if there were any testing on each lot and if there were any cultures that's in any of those lots.

Janet Woodcock:
There's been - (Brad) do you want to talk about that? (Brad Leissa) is here with us.

(Brad Leissa):
Yes hi, this is Doctor (Brad Leissa). I'm a Medical Officer here at FDA. And FDA has performed, as Doctor Woodcock was saying before, has analyzed several samples of these - of the suspect lots.

To date we have several samples of the what's referred to the 08102012 at 51 methylprednisolone acetate lot which is showing microbial growth. And we have shared that with CDC for identification.

And then also of the other suspect lot of the 06292012 at 26 of the methylprednisolone acetate. So we have several samples from those suspect lots that are positive.

Woman:
But not the other lot, not the last one?

(Brad Leissa):

From the other lot at this point we still have cultures that are pending on that. But we don't have any results yet to announce about them.

Woman:
Thank you very much.

(Brad Leissa):
You're welcome.

Janet Woodcock:
And this is Janet Woodcock. If you go on the update on fungal meningitis page on the FDA drugs page, at the bottom would be the advice to healthcare professionals. There's a section called related information.

And under that there is a bullet. And it says patient notification letter. So that is where that is located.

Leticia Davila:
This is CDC. We will also link the Website to resources on our call - for the call today.

Coordinator:
Doctor (Norman Casto) your line is open.

(Norman Casto):
Thank you. I'm looking at the list of NECC customers. And I was very surprised to see a surgery center on there that told me they didn't use any CC products when I called them about two weeks ago. When was the recall issued?

Janet Woodcock:
The entire recall was on October 6.

(Norman Casto):
Okay so...

Janet Woodcock:
CDC operated the recall. But our list that was posted on Monday was not the correct list. But on Tuesday we put up the correct list. So make sure you're looking at the correct list.

(Norman Casto):

Well this, I did a search on Google. And this is the list that came up. How do I tell which list is which?

Janet Woodcock:

If you go in the FDA Web page you can make sure that you have our - just go fda.hhs.gov. And get on - get that list.

(Norman Casto):

Okay. Then also it was...

Janet Woodcock:

fda.gov, pardon me, yeah.

(Norman Casto):

Yes fda.gov.

Janet Woodcock:

Yes.

(Norman Casto):

At the list, the Web page cannot be found.

Janet Woodcock:

The list can't be found or the Web page can't be found.

(Norman Casto):

FDA.gov, I'm getting Web page cannot be found.

Janet Woodcock:

Oh okay.

Tom Chiller:

Are you putting www in front of FDA?

(Norman Casto):

No.

Tom Chiller:

Try that. See if that helps.

(Norman Casto):

Also the list is alphabetical, but it is also including articles. So its name begins with the, it's listed under T.

Janet Woodcock:

Yes we list it as how the shipping entity named itself to be shipped to. The add - you know, the name of the entity. And it is sorted by state though, if you're looking in your particular state, you can look at it by state and find it there.

(Norman Casto):

Yes. I did look by state. But as I say, it was - although the facility's name begins with an A, it had “The” in front of it. So it was alphabetized in the Ts.

Janet Woodcock:

Right.

(Norman Casto):

I'm in the FDA site. And where do I go from here.

Janet Woodcock:

Okay what would be best, here's a phone number is 855, okay.

(Norman Casto):

855.

Janet Woodcock:

534.

(Norman Casto):

534.

Janet Woodcock:

3784.

(Norman Casto):

3784.

Janet Woodcock:
If you call that number, you can get one of our pharmacists who can walk you through this. And we can get the information you need.

(Norman Casto):
Okay. One other question, in the future are there going to be conspicuous labels on products saying that they don't contain preservatives?

Janet Woodcock:
That is true for FDA-regulated products. But I can't, you know, comment on products that are compounded. Those have - are subject to the local board of pharmacy rules.

(Norman Casto):
Yes. Hopefully you'll move forward on that with the states. I know it's listed in the package insert. But I'm talking about something more conspicuous.

Janet Woodcock:
Yes.

(Norman Casto):
Okay thank you.

Janet Woodcock:
FDA regulated injectables have something that's more conspicuous so thank you.

(Norman Casto):
Yes.

Coordinator:
(Sharon Demato) your line is open.

(Sharon Demato):
Yes hi. We currently use a compounding pharmacy. It's not NECC. And we do get products that we are using for epidurals, specifically preservative free.

However, we get a sterility flow sheet indicating the lot has been sterilized. So I'm just wondering if that's sufficient information for us to continue with a sense of confidence?

And then again, and that's Question 1 backed up with did NECC provide this kind of information that the medications in question were and did past sterility testing?

Janet Woodcock:
Yes this is Janet Woodcock. I can't - I don't know what NECC sent along with their shipments. But I can tell you, you know, we regulate all the sterile injectables in the United States except the ones that are made by compounding pharmacies.

And a sterility assurance really has two parts. One is the process, right, which has to be, you know, aseptic processing, which is a - it's more than just sterilizing or sterile filtering something at the end of the day.

That's the second part is to ensure sterility in testing for the end product. But a sterility assurance also involves the process. So I think an end product sterility test pass is only as meaningful as what test was done.

How statistically valid was the sample that was taken and so forth? And even then it's not a full assurance of sterility. It is only in use in conjunction with proper procedures during the sterile manufacturing.

So I know that per individual healthcare facilities, looking into the sterility practices of their suppliers is difficult. But those are the pieces that go into that.

And possibly you could contact the Board of Pharmacy in the state in which that compounding pharmacy is located.

(Sharon Demato):
Okay I appreciate that. Thank you.

Coordinator:
(Alan Oaken) your line is open.

(Alan Oaken):
Yes hi, thank you. I have three sort of related questions. I appreciate it. We're an orthopedic surgery practice.

First question is of the five joint infections, were all of them associated or any of them associated with anything but the three tainted lots?

My second question is in terms of notification of patients, I believe I read that it was sort of up to us on how we best handle it. Can our Website be used for that just because we're talking about a lot of - we never used the tainted lots. But we've used other NEC injectables.

And there's a lot of people to notify and who are going to get nervous and scared and all that. And I'm just wondering if the Website is acceptable?

And thirdly, for patients who are preparing for surgery who are asymptomatic but have received an NECC injection, do you have any suggestions for testing for pre-op patients?

Tom Chiller:
Well this is Doctor Chiller. I'll take the, at least the first one and maybe a stab at the third. And then Doctor Woodcock can answer.

As far as the five joints that have been reported so far, yes these are all from patients who have received one of the three lots of MPA product. So again, all the cases to date that we have that have been reported to us at the CDC by state and local health departments are from those three lots of MPA product.

And if you're - and so for the third question. If you're talking about, I guess you're talking about current preoperative conditions. And again, I don't really have a comment per say about current preoperative conditions because I assume no one should be using any products from NECC.

(Alan Oaken):
That is correct. We pulled those October 3, yes.

Tom Chiller:
Perfect. So again, what we're concerned about and what FDA is concerned about is the sterility of products from NECC particularly.

(Alan Oaken):

Right so, but I guess where our concern is for patients who are going to undergo for example a hip replacement. Obviously if someone has a potential for an infection like this, it would be severe outcome potentially.

But if a patient comes and is concerned and they're asymptomatic. Obviously normally we would not undergo anything - any testing other than standard pre-op testing, you know, the blood work and things like that.

Is there anything extra we should be doing for these patients? Hip aspirations or anything like that to assure the patient that they're going to be okay?

Tom Chiller:
So you're saying, so let me - are you saying a patient who would have received one of the contaminated lots of MPA maybe a month or two ago and now comes in for surgery?

(Alan Oaken):
Yes, although we didn't use the - of the three tainted, it would be, you know, the Kenalog generic or the Celestone.

Tom Chiller:
I mean our current clinical advice is if one of the pat - if a patient has received, certainly if a patient has received one of the three lots of MPA and has symptoms, then we of course would be aggressive in trying to diagnose and evaluate that patient.

And as we've said, if they're asymptomatic, the risk begins to go down as time passes. And we sort of feel that the risk beyond that six-week period is extremely low.

And so if they're asymptomatic beyond that six-week period, we feel they're at extremely low risk. But if they were within that six-week period, give or take and then I would encourage a diagnostic workup to be done prior to them getting surgery.

I think for non-MPA three lot products, again I think we're concerned about patients with symptoms of some sort of infection.

So if you're dealing with an asymptomatic patient two months out of the injection from a non-MPA three lot implicated product who was completely asymptomatic. At this time, we're not seeing any reason for anything special to be done.

(Alan Oaken):
All right, very helpful, and on that third question?

Janet Woodcock:
All right, on the question about can you just put something on your Website? We've been asking people to advertly follow up perhaps by a letter that we suggest.

Eliciting from patents because particularly say with orthopedic injections, they may have had a sore knee. And now they have a sore knee again. And we feel that more avert follow up will be helpful.

However, we recognize that, you know, there's a balance between alarming the patient and following up. So we had suggested sending a letter to patients who were exposed during the summer to these products.

(Alan Oaken):
Thank you. I mean, and you are right. I mean it is causing pandemonium in our community and probably throughout the country. And when people are such low risk, and I certainly do understand, you know, your phrase abundance of caution.

But it's - it is causing such extreme interest by everyone and phone calls and so it's just, thank you. That's very helpful.

Janet Woodcock:
Good.

Coordinator:
Doctor (Craig Smith) your line is open.

(Craig Smith):
Hi, I'm Doctor (Craig Smith) in Georgia. And I wanted to follow up on the same questions. The FDA makes a recommendation. But our state pharmacy board makes it a mandate.

And following up with patients that got intravenous solutions such as cardioplegia or potassium or one of the other drugs seems to be a very different situation of unknown consequences.

The FDA letter refers specifically to symptoms and injections into a local site. You know, when we notify the patients of intravenous, receiving intravenous medicines, how - it is pandemonium.

How are we supposed to follow up every single patient that has every single symptom? It becomes hundreds or thousands of patients, which is not feasible.

Janet Woodcock:
Well we recognize that you have to use your clinical judgment, as you heard from the CDC, as time goes on past this outbreak, we perhaps develop more confidence that there aren't other infections emanating from this.

We suggested a letter be sent to the patients. And if your clinic was giving or your hospital setting was primarily giving intravenous medications, then you could tailor the letter to the kind of symptoms that patients might experience, particularly unexplained fevers for example. And not be, you know, having everybody who has a cold come in and call you.

(Craig Smith):
That sounds very heroic. But there is no past clinical experience. There is no literature to base anything on.

Janet Woodcock:
I know.

(Craig Smith):
There is no, you know, FUO-type presentation or anything. What it does is opens up an entirely subjective can of worms with no scientific basis to fall back on of any kind.

Janet Woodcock:
Yes we recognize...

(Craig Smith):
Not to mention the legal risk and everything else that goes along with it. I don’t know if there's any literature, or I haven't found any literature that would even support intravenous syndrome in a similar situation.

Janet Woodcock:

Yes and we're in uncharted territory. And we recognize that. And we recognize the burden this is putting on the healthcare system. But we also are pointing out that we have no assurance that these products are administered intravenously to patients were sterile.

(Craig Smith):
Then I would suggest that the CDC and FDA collaborate and provide us with a suggested letter to send to patients receiving intravenous products. Because if we have no literature, science or recommendation to base it on, then that means every single facility in the country is sending out their own letters of whatever without any background or anything. Which is totally erratic.

So that means they'll be no routine follow up. They'll be no anything for any of these patients or any of these facilities. And it puts everybody at a tremendous medic legal risk when an FDA requires us to contact people for information that we don't know what to ask and we don't know how to interpret.

Janet Woodcock:
Well thank you. We will consider what we can do about the intravenous products. Thank you.

Coordinator:
(Margaret Neil) your line is open.

(Margaret Neil):
Yes I have a question for, or a couple of questions for Tom. Pardon, the first one many seem very simplistic. Regarding the asymptomatic patients guidance, is Option 1 essentially or really the prior guidance, which was watch closely and LP if symptoms?

Tom Chiller:
Yes thanks for that. Absolutely, Option 1 is essentially the prior guidance that where we're basically saying watch closely. Development of symptoms, if they or symptoms worsen or persist then have low threshold to LP.

(Margaret Neil):
Okay great and then my second and third questions, which are short. When we were at ID week we heard from a few of the clinicians from Roanoke. It was most interesting to see the group of persons that had an initial LP that was negative for white cells.

And subsequently there were, as I recall, two of 70 who developed symptoms and on repeat LP now had CSF pleocytosis. My question to you is whether you have any similar data that is accruing that you could share?

And then the third question is a lot easier, which is we were hearing about still single digits, but more *Cladosporium*. Can you make any comment on that?

Tom Chiller:
Yes thanks for those two questions. We have heard, and you point out the Virginia experience, we have heard of a few patients like this who have negative lumbar punctures or CSF results, meaning less than five cells.

And then have returned with either worsening or persistent symptoms. Have had a re-examination of their CSF, and have had greater than five cells. And have been put on treatment. That is still a small number of patients. But it is occurring. And we have heard of it.

I've even heard of one that has had two negative LPs and then the third LP was positive. So that's why we're, you know, we are suggesting that we remain vigilant with these patients.

And we continue to monitor them closely. I think if all - in all of these cases symptoms have persisted or worsened or developed. And so we are continuing to suggest you use that as a guide.

As far as more *Cladosporium*, the - we - as we've said, we've reported one case of *Cladosporium*. We have a few other cases that where mold is still being identified.

And again, the majority I think we're up to 50, 54, 55 plus cases have been *Exserohilum*. So we still feel strongly that this is mainly an *Exserohilum* outbreak.

And so we're cautiously evaluating other molds that grow because, you know, unfortunately *Cladosporium* is a common contaminant in laboratory settings. And so we just want to make sure before we label a patient as having an infection with a different mold species that we're pretty confident that it is indeed causing the infection.

We realize that this indeed could be a multiple organism outbreak. And so we're taking just all the precautions that we can to make sure we confirm infections before we report them.

Leticia Davila:

Operator at this time how many questions do we have in the queue?

Coordinator:
At this time there are no questions.

Leticia Davila:
Thank you. Thank you Doctor Schaefer and Doctor Chiller and Doctor Woodcock for providing COCA audience with such a wealth of information.

As a reminder, excuse me, on behalf of COCA, I would like to thank everyone for joining us today with a special thank you to the presenters.

If you have additional questions, please email us at coca@cdc.gov. Again that email address is coca@cdc.gov.

The recording of this call and a transcript will be posted to the COCA Website at emergency.cdc.gov/coca within the next few days.

There are no continuing education credits for this call. Meningitis resources for clinicians are available on the COCA Web page. Go to emergency.cdc.gov/coca. Click COCA calls, and follow the links for the meningitis call.

To receive information on upcoming COCA calls, subscribe to COCA by sending an email to *coca@cdc.gov*. And write “subscribe” in the subject line. CDC launched a Facebook page for health partners. Like our page at Facebook.com/cdchealthpartnersoutreach to receive COCA updates.Thank you again for being part of today's COCA call. Have a great day.

Coordinator:
This concludes today's conference call. You may now disconnect.

END