FDA MEDIA BRIEFING ON HEPARIN

Moderator: Julie Zawisza
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1:30 p.m. ET

Coordinator: Good afternoon, and thank you all for standing by. All participants will be able to listen only until the question and answer session of today's conference call. Today's call is being recorded, if anyone has any objections you may disconnect at this time. And now I'll turn the call over to your first speaker for today Miss (Julie Zawisza), ma'am you may begin.

Julie Zawisza: Thank you. Good afternoon ladies and gentlemen. I'm Julie Zawisza the Assistant Commissioner for Public Affairs with the FDA, and wanted to thank you for joining us on our call today. We had said to you last we that we'd provide regular updates on our Heparin investigation, and that's just what we're going to do right now. It's been about a week since we talked to you and we have a number of developments we'd like to tell you about.

Here to talk about those is Dr. Janet Woodcock who's our newly appointed director of the Center for Drug Evaluation and Research here at FDA, and congratulations Dr. Woodcock.

Dr. Janet Woodcock: Thank you.

Julie Zawisza: On your new appointment. And then we'll go to – after her remarks we'll go to a question and answer session and I'll introduce some other people at that time. I'd like to turn it over to Dr. Woodcock.

Dr. Janet Woodcock: Thank you (Julie). Well as you're well aware there have been serious adverse events associated with Heparin marketed by Baxter Healthcare Corporation in the United States.

The active pharmaceutical ingredient in this product comes from the Changzhou SPL plant in China. FDA conducted an inspection in this plant and we obtained 28 API samples. And today what we're announcing is that using our screening tests we found that 20 of these samples had Heparin-like contaminant.

So today FDA is announcing a number of preventative steps that we're putting in place at America's borders to prevent the entry of potentially unsafe Heparin products.

First, as a precautionary measure the Changzhou SPL plant has been added to an existing import alert, alert number 6640. Although the Changzhou plant agreed not to import product into this country, there have been no actual restrictions that would prevent them from importing. And this alert will detain all Heparin products they might ship in the future.

Second, FDA issued an import bulletin Monday to our field investigators alerting them to consider all products containing Heparin as products of interest. This alert tells investigators to pay special attention to all Heparin products slated for entry into the United States. They will be stopping all Heparin products slated for import and assuring that manufacturers are testing them or we will be testing them ourselves using the following approach. [Editor's note: testing only Heparin API]

First, FDA has received commitments from manufacturers who currently supply injectable Heparin Sodium to the US market to test their active

pharmaceutical ingredient products for potential contamination using the two sophisticated tests that we put out last week.

These tests, proton nuclear magnetic resonance spectroscopy and capillary electrophoresis are the ones we made available on our website.

Some of these manufacturers import a Heparin API from other countries. Others use domestic API sources.

In addition to the commitments received by the Heparin injection manufacturers companies that import crude Heparin from overseas to manufacture the API in the United States have also committed to test those APIs for contaminants and the crude Heparin.

Selectively the companies making these commitments represent a substantial part of the overall Heparin market and their agreement to conduct full testing and report all results to FDA will really improve our safety net, and I think yield major patient safety benefit.

Manufacturers making this test commitment will be able to import their API from overseas sources without delay to avoid shortages in supply of Heparin which would also be a very dangerous situation for the patients.

Additionally, FDA issued a sampling assignment to our field investigators aimed at Heparin Sodium API made by manufactures who’ve not committed to doing this sophisticated product testing. FDA will hold the sample and test their Heparin Sodium APIs to determine if the contaminant is present. And products that are contaminated will be refused entry and FDA will request their destruction.

We are continuing to monitor adverse events that are occurring in the United States. We've – since Baxter's expanded recall that occurred on February 28 we've received no reports of death that have occurred since that time that related to allergic reactions and to Heparin.

We have received two reports of allergic type reactions that have occurred since that recall, and we are further evaluating both of those reports.

All these measures have one goal in mind to ensure that healthcare professionals and their patients can have full confidence that a potentially life saving product like Heparin is safe to use.

Thank you and we'll turn it over – back to (Julie) for questions.

Julie Zawisza: Thanks Dr. Woodcock. So before we go the phones I wanted to share with you some information that we think you'll find helpful. We have three graphics that we've developed that we've just posted on our website. And these graphics illustrate, describe to you key components of our investigation. There are three sets.

The first one describes the actual analysis of the contaminated samples. And the third – the second ones describes how we scrutinize diverse events and how we go from a large number to a smaller number as sift through and analyze those reports. And third, how we issue import alerts.

Now I invite you to check our website, look at those graphics. There may be two graphics not three. I said three. It is three, I was correct the first time. So later on in the discussion maybe you can do that.

Before we go the Q & A I wanted to introduce a number of folks who are with us today with Dr. Woodcock and also on the phone. And I'm going to give you all of their titles, because I think it's important that you understand in a complex investigation like this how many people get involved and the range of expertise that's needed.

In addition to Dr. Woodcock we have Steve Silverman who's the Assistant Director of our Center for Drugs Office of Compliance. And we have also in the Center for Drugs Ann McMahon who is the acting Director of the Division of Adverse Event Analysis II.

Also in the Center for Drugs we have Dr. Moheb Nasr who is the Director of the Office of New Drug Quality Assessment. And finally in the Office of Center for – excuse me in the Center for Drugs we have Rick Friedman who is their Director of the Division of Manufacturing and Product Quality in the Office of Compliance.

And lastly, we have, but not least Dominick, we have Domenic Veneziano, a very important person, Director of Import Operations and Policy in the Office of Regulatory Affairs.

So I know I gave you a mouth full of titles, but again, I think it's important that you see the breadth and the scope here. With that let's go to the phones. And let me remind you that we need your name and affiliation, one question and one follow-up please. Ready to go. First question please operator.

Coordinator: At this time if you'd like to ask a question please press star 1 on your touch tone phone. To remove your question you will press star 2. Once again, in order to ask a question you will press star 1 on your touch tone phone.

Julie Zawisza: Someone must have a question.

Coordinator: Our first question comes from Peggy Peck with MedPage Today, ma'am your line is open.

Peggy Peck: Thank you. Thank you for taking the question. This is Peggy Peck) with MedPage Today. I want to understand what exactly you're saying about locating this in the facility in China. Do you – have you identified how the contaminant made it's way into the API there or where are you in that?

Dr. Janet Woodcock: No, we have not identified that. We are continuing to nail down the identity of this contaminant, and I think when we have completed that we have multiple laboratories around the country working on this issue and I think we're very close. When we have completed that I think it will help us in understanding how this may have gotten into the Heparin. But we have through our testing of the sample we collected there we know the contaminant was present in those APIs in China.

Peggy Peck: And on follow – there are other facilities in China that are sourcing Heparin, have you found this then contaminant at other plants in China?

Dr. Janet Woodcock: What we're doing now is we'll be either testing or getting results from manufacturers who are testing any APIs that are imported from China. So there is a large amount of movement of Heparin around the world. And we understand that world wide there is testing going on, but what we're announcing today for the US is that at our borders either we will be testing or we will be receiving test results from import manufacturers who are importing these APIs so that we'll get a much better picture of whether there's any contamination existing and then we can trace it back to where it might have originated from.

(Julie Zawisza): Thanks, next question.

Coordinator: Our next question will come from David Greising with the Chicago Tribune, your line is open Sir.

Julie Zawisza: Go ahead David.

David Greising: Thank you. To follow up on that question, have you in coordination with the Germans and there was this related Japan case, have you found whether this same - the suspect ingredient is present in those cases?

And a second and different question, I was hoping we could get some definitive numbers on deaths in particular, because after the last call when we went to Baxter they had a far different number than – they were sticking with four deaths, and they raised questions as to whether these really are even Heparin-related deaths is the four that they are acknowledging. And I'm wondering where – whether you all have aligned the death count on it.

Dr. Janet Woodcock: Too get – we'll have to get back to you on this – or back to everyone on this issue of deaths. I mean, there are a number of deaths – it says here with administration of Heparin versus the number that have thought to be causally related there's this whole cascade of understanding about the death. Anne do you have any comment on that?

Ann McMahon: I would just say that we're evaluating the deaths associated with Heparin and we've – it's not been – we don't have enough sufficient information to directly link the deaths.

David Greising: Well, I think some of the confusion was that the number you put out, I think it was 28, [Editor's note: 21] went back to before the Heparin in question was even manufactured much less shipped to the United States. And so there – it was a little bit confusing as to why – because we know that there are, you know, even with perfectly good Heparin there are people who have adverse reactions and they die because of it.

And I'm just wondering why your timeline for the Heparin related deaths go back as far as it does.

Dr. Janet Woodcock: All right. Well we will put something up on our website that is clear about when we're – in different evaluation periods and how many associated deaths were observed so people understand that.

You have to understand that with the manufacture of Heparin from APIs it's moving through different pipelines at different timeframes and so we do have to – we're looking very carefully at this. But we will do something so that people understand the numbers.

With respect to your first question – which was a good question -- we are working with the regulatory authorities in other – in Germany for example to follow-up on the testing of that - the lots that were implicated in those adverse events. But we don't have anything to say about that today.

Julie Zawisza: Thank you, next question.

Coordinator: Our next question comes from Walt Bogdanich with The New York Times, Sir your line is open.

Walt Bodanich: My understanding is that when your inspectors had visited the consolidators in China for Chungzhou SPL that they did not then pursue their investigation up stream to the workshops, why not?

Rick Friedman: This is Rick Friedman. The inspections that FDA generally engages in are inspections of active pharmaceutical ingredient manufacturers. And as you go earlier in the supply chain for natural ingredients such as this it really ends up being the USDA equivalent in China that would actually inspect starting materials or the animals and, you know, the very early source materials for a drug product such as this.

So, you know, we've had certainly a lot of discussions with a consolidator as well as the API manufacturer regarding the quality of their incoming starting materials. And that's in fact how it's regulated.

We asked API manufacturers and the consolidator, which is an intermediate manufacturer who we often don't we inspect. In this case we did visit these consolidators. We asked them to characterize the purity and quality of the incoming raw materials to assess whether they're suitable for use in manufacturer. So that's how FDA assesses it from our end.

Walt: Yes, but my question is why did you - I mean you don't normally inspect consolidators, but you went there. My question is why did you not go to the -- continue on since this is an around the clock massive operation with all sorts of people sitting here now at this press conference?

I, you know, I would like to know why you did not, you know, in an effort to find the cause of this, go further up the supply line. Are you relying on information you're getting from the Chinese equivalent of the USDA? Is that

what you're saying? I mean why did you not do it personally -- send your investigators over there?

Steve Silverman: This is Steve Silverman. And the short answer is no we are not simply relying on information from our Chinese counterparts. We're engaged in a very active investigation and we are looking at all possible causes of this adverse event, including actions associated with the consolidators and upstream suppliers.

I think as Rick pointed out, though, our area of expertise and our typical approach when we engage on adverse events, is to focus our energy on drug manufacturers. In this case, SPL in China. That is where we began our investigation, and that is where we focused our resources initially and energetically.

The fact that we haven't to this point taken a look in terms of feet on the ground inspections of the consolidators doesn't mean that we aren't paying attention to their roles in these events and working with our counterparts within this government and within our counterparts in China to gauge the potential relationship of their activities to the contamination that we've seen.

Walt Boganich: I understand. One last question…

Julie Zawisza: I'm sorry. We've got to move on, Walt. Very sorry. Next question please.

Coordinator: It looks as though our next question comes from Lauren Neergard with the Associated Press. Your line is open.

Lauren Neergard: Hi thanks. Could you all give a breakdown on how many manufacturers have said they're going to do the testing themselves, how many that (lead) that you will all will then have to be testing at the border, and why you think that the

importers testing themselves will be reliable -- what you'll be doing to check that they're actually doing the testing and not fudging the results.

Steve Silverman: Well the answer is that they're going to be providing their test results to us and that we expect them to test according to the methodologies that we've developed. And we'll be able to evaluate whether in fact they did test according to those methodologies.

With respect to how many firms, we have at this point written commitments from five finished product manufacturers and (API) distributors. These firms collectively represent a major portion of the heparin product model language in the United States. And so we feel that beginning with these firms and getting commitments from them, which they very readily provided when asked, we'll have assurance as to the quality of substantial part of the (API) supply.

Obviously if further supply comes in from firms that have not yet provided written commitments but the firms are interested in providing written commitments so that their product also can pass through, we are happy to have those conversations with these firms. We hope that they'll follow that pathway and that will further help us to in a safe way assure a supply of heparin (API) coming into the country.

Lauren Neergard: Are you going to be doing spot checks at the border to make sure that the written commitments are being followed up on correctly?

Domenic Veneziano: This is (unintelligible). I don't think the - the written commitments won't be done at the border. It could be followed up in the domestic inspection side of things, but that's something that we would have to address later on when we start seeing reports come back.

Julie Zawisza: Thanks, Dominic. Next question please.

Coordinator: Our next question comes from Jon Rockoff with the Baltimore Sun. your line's open.

Jon Rockoff: Thanks. So what's the status of the investigation with regards to the plant in Wisconsin? Are you still looking at them or focused elsewhere?

Steve Silverman: It relates to an open investigational matter and we prefer not to comment on it at this time.

Julie Zawisza: That was Steve Silverman from the Center for Drug Office of Compliance. Next question please.

Jon Rockoff: Can I ask a follow up?

Julie Zawisza: You can. You may.

Jon Rockoff: Sure. Thanks. I mean how would you characterize the focus of your investigation? Would you say it's more focused on China than elsewhere? I mean can you at least do that?

Rick Friedman: Our investigation has been comprehensive. We've looked all aspects of…

Jon Rockoff: I mean now. I mean now.

Rick Friedman: Well we continue to look at all possible sources of the contamination. And until we get to root cause we'll continue to work vigorously internally as well

as external stakeholders such as the companies involved with this issue to determine the cause of these adverse events.

Julie Zawisza: That was Rick Friedman in the Center for Drugs. Next question.

Coordinator: Our next question is coming from Heidi Splete with Family Practice News. Your line is open.

Heidi Splete: Hi. Thank you for taking my question. What should doctors be telling people right now who might be needing heparin or knows someone who needs heparin. What should they say when people come in and say, “I'm scared. What should we do? Should we worry?”

Janet Woodcock: Well, you know, I've had calls and emails from people who know me -- this is Janet Woodcock with CDER -- asking me the same question. And I think doctors should reassure patients. You know, we have not - since we've had the recall we have not received a report of a death from this. We've received a couple of allergic type reactions, but as Steve said, that - there is a background of this that we see.

So we’re not seeing a cluster of events like we saw earlier. We are committed to looking every day at the adverse events that we report. We're also committed to putting this testing and this safety net at the border into place.

The other thing you should please tell doctors -- if they have a case, please report it to the FDA, because that will be of tremendous help to them. And if they would note the manufacturer and the lot number of the portfolio associated with it and put it into the report and put as much information into the report as possible so we can evaluate it, that would be extremely helpful to us.

Julie Zawisza: Yes, this is Julie Zawisza. We really want to thank you for that question because in the midst of this investigation, all of the detail and the drill down into all the work we're doing, we never want to lose sight of the fact that what this really is about is patients getting a safe product and doctors and patients having good information from the FDA on treatment.

So we really appreciate you getting out that message. Thanks and we'll take the next question.

Coordinator: Our next question is from Ricardo with the Los Angeles Times. Your line's open.

Ricardo Alonzo-Zaldivar: Hi. Yes, Ricardo Alonzo-Zaldivar with the Los Angeles Times. Thank you.

Julie Zawisza: And we can say it and we can spell it.

Ricardo Alonzo-Zaldivar: All right. Well - excuse me. My voice is a little…

Julie Zawisza: We can hear you.

Ricardo Alonzo-Zaldivar: …kind of raw. But anyway, I just wanted to ask you, what do you - what more do you know about this contaminant now than a couple of weeks ago when you first told us about it? Can you tell us a little bit more? What do you know now that you didn't know at first about it?

Janet Woodcock: Well we have a huge number of additional test results. We are testing this every which way that the chemist could possibly dream of, to separate and test this compound. And we are - as I said, I think we're very close to nailing this

down. But this contaminant is a complicated biological molecule or molecules, and so figuring that out when it's contaminating a complicated biological molecule, which is heparin, has been a real challenge - a real chemistry challenge.

But we have I think the - some of the best minds in the world working on this, and we know a lot more about this. It's all too technical to put in the newspaper, because it has to do with spin signals on NMR and all kind of stuff that I don't think your readers would be interested in.

But the point is, we are coming close to understanding what this is, and I think when we understand it, that's really going to help us figure out how it got in there.

Ricardo Alonzo Zaldivar: But how is it a molecule has toxic properties to it? Have you identified what that is?

Woman: No we haven't linked this contaminant to the adverse reactions other than the fact that the lot - for example, even the API lot that we - some of them that we got from China and tested, those were - and were contaminated, those were the lots that were present in the finished product that caused adverse reactions, okay?

So we have sort of guilt by association, but we don't have a mechanistic link saying that these compounds caused it. They may simply be a marker for something else that's in there that actually is causing this reaction.

Julie Zawisza: Let's take the next question please.

Coordinator: Our next question comes from Justin Blum with the Bloomberg News. Your line is open.

Julie Zawisza: Hi, Justin.

Justin Blum: Hi. Thanks for taking my call. Someone who didn't identify himself mentioned that there were five manufacturers of either finished product or the active pharmaceutical ingredient who agreed to do the testing. Can you name those five? And beyond those five, how many more are there?

Steve Silverman: Well this is Steve Silverman and I was the person who mentioned the five manufacturers of the finished product and distributors of active pharmaceutical ingredient. And the short answer is that at this time we're not going to name them, because we do not yet have permission from those firms to share those names publicly. But we will certainly make inquiries. And if we get their permission then we'll be happy to share that information.

We think that they represent a substantial portion of the market for both finished product and (API). I cannot give you a definitive percentage, but we have spent a lot of time thinking about who the major players in this area are, and we think that this group represents those major players.

Justin Blum: And Steve Silverman, what's your title?

Steve Silverman: I'm the Assistant Director of the Office of Compliance in the Center for Drug Evaluation.

Julie Zawisza: Thank you. Next question. That was your two, Justin.

Coordinator: I'd like - our next question will be coming from Jennifer Smith with FDA Week. Your line is open.

Jennifer Smith: Hi. Actually I have a whole slew of questions that a bunch (eventually open). But I guess to start off with two.

Julie Zawisza: We can only give you time for two. We have a lot of people in the queue.

Jennifer Smith: I understand that. Okay, can we just start of here -- there's a mention about how FDA doesn't usually inspect consolidators. Can you just give me a better idea of what - really a better definition of consolidators, and that this is something that's going to - this incident now -- this going to maybe push FDA resources or you think (unintelligible) FDA to take a closer look at consolidators in China or just abroad?

Steve Silverman: The consolidators are not always part of the active pharmaceutical ingredient supply chain.

Jennifer Smith: Okay.

Steve Silverman: In this case, a lot of different lots are put together and consolidated and are then subjected to a conservation process. Only one step in this case. And they are sent on to the retroactive pharmaceutical ingredient manufacturer for several purification and inactivation steps are among - purification steps, including inactivation and oxydation and things like that.

So that's really the consolidator role in the supply chain to consolidate lots and produce a precursor…

Jennifer Smith: Okay.

Steve Silverman: …to that the (API) manufacturer may use.

Jennifer Smith: Okay.

Julie Zawisza: I got to keep going here. The - did you finish your answer? I didn't want to cut you off? I'm sorry I - we've got to keep going.

Jennifer Smith: My second question wasn't answered, though.

Julie Zawisza: Which question wasn't answered?

Jennifer Smith: And that's was particularly whether now FDA is going to be paying more special attention to consolidators after this incident.

Julie Zawisza: Isn't this case-by-case?

Steve Silverman: This is Steve Silverman. We're making that decision on a case-by-case basis. Here It's obviously an item that we're interested in, but with respect to (unintelligible) prospective cases, it's impossible to say in the abstract.

Julie Zawisza: Thanks. Next question please.

Coordinator: Our next question comes from Rob Foreman with CBS Early Show. Your line is open.

Rob Foreman: Yes, thank you. Just a clarification of how well you know what you are looking for. You spoke of how complicated the molecules or molecules are, figuring out all being a challenge and so forth. Are you confident that a lot that might be causing the problem might go through because you're not quite sure yet what you're looking for? And I have a follow up.

Julie Zawisza: Good question.

Janet Woodcock: Yes, that's a good question. We aren't 100% confident, but we have a very high association of this signal with the loss and the products that caused the problem. Okay, so we are pretty confident, although maybe what we're detecting isn't the exact molecule, it's in there somewhere and we can detect this contamination. We're confident that we can detect this contamination. Okay, does that help you?

Rob Foreman: I think so. Yeah, I was just wondering whether it was a wide-open situation and when what you're looking for is, as you said, maybe not nailed down 100%, but you know it's there when you see something.

Janet Woodcock: Yeah, we're very close to knowing exactly what these molecules are. What we don't understand is how they cause allergic reactions. That's what we don't understand and because of the nature of allergic reaction, there could be a very small piece in this contamination that we detect that's actually causing the allergic reaction; okay, if you follow me.

Rob Foreman: In other words, you're confident that it's part of the array that you're finding, but what part of the array that you don't know?

Janet Woodcock: That is right. That's fair.

Julie Zawisza: Thank you.

Rob Foreman: And the follow-up would be how much product are you testing, is it some from every single lot; is it some from every single shipment, how does that

break down and what confidence does that bring that you know you're catching wherever it might be coming from?

Janet Woodcock: Well, yeah, we'll have – Domenic's going to say something. I would like to emphasize that there is now a worldwide testing effort going on. Every country practically, you know, that is a developed country is getting their manufacturers to test and so we're going to have, because we put those test methods out very early, we're going to have a lot of information and get a much better understanding of this globally what the Heparin supply is like in a week or so.

Domenic Veneziano: And in terms of the assignment that we issued, every shipment of API Heparin coming into the country will be tested one way or the other, as Steve Silverman mentioned by the companies themselves or by FDA.

Julie Zawisza:: That was Domenic Veneziano, and then Dr. Woodcock. Next question?

Coordinator: Our next question comes from Lynn Peterson with Trends in Medicine. Your line is open.

Lynn Peterson: Hi, can you give us an update on what you know about this contamination in other countries in Germany and Japan and are there any other countries that have spotted it?

Janet Woodcock: As we announced what was going on in Germany and we are working with them to see if the contaminant that we identified is present within those batches. Moheb do you know anything about the Japanese -- I think that was just a preventive measure.

Moheb Basr: Yes, this is Mohen Nasr. We are working very closely with our international regulatory authorities to protect all prospective material and testing in Germany started a few days ago and we talked to our Japanese colleagues two nights ago and they are going to start to conduct some testing to make sure that the Heparin (unintelligible) from (unintelligible) Japan is safe.

We do not have specific test results, but we continue to provide them with information. In addition, we also have to do 15 (unintelligible) called (unintelligible) in Germany and other countries and our own laboratories.

Woman: Thank you; next question.

Coordinator: Your next question comes from Jennifer Corbett with Dow Jones. Your line is open.

Jennifer Corbett: Yeah, thanks. The question I had is just logistically because you said you're going to be stopping, you know, all the shipments at the border. Now the countries that have agreed to test, what happens -- I mean I'm assuming that the testing is not occurring at the site where it's imported. What is it going to be released to the companies for testing on their own sites?

Domenic Veneziano: That is correct; this is Domenic. The shipments, as they come in, will be allowed to move to destinations, so the companies that they're going to will be able to receive them, perform the tests and provide the information back to us.

Julie Zawisza: Thank you; next question.

Coordinator: Our next question comes from Daniel Poppy. You line is open.

Julie Zawisza: Who are you with, sir?

Daniel Poppy: Geneuse. [Editor's note: may not be proper name] Thanks. The five that have committed, do you already have results and are you satisfied with what you've seen?

Steve Silverman: No, we don't yet have results. These commitments are very, very recent.

Julie Zawisza: That was Steve Silverman.

Daniel Poppy: Can you say where these five companies are based?

Julie Zawisza: We already said we weren't able to name them at this time.

Daniel Poppy: Well, are they all foreign or is it someone domestic?

Julie Zawisza: I don't think we're ready to do that.

Steve Silverman: What I can say is that these are all firms that have a significant domestic presence in the US and all firms that are receiving their Heparin ingredient at least in part from abroad.

Julie Zawisza: Thank you; next question.

Coordinator: Our next question comes from Marc Kaufman with the Washington Post. Sir, your line is opened.

Mark Kaufman: Thank you.

Woman: Hi, Marc.

Marc Kaufman: Hi. Early on in one of your earlier teleconferences, there was some discussion as to whether or not the contaminant that was part, that might have been part of the manufacturing process or if it was something that was kind of an adulterant that was added. Do you have any additional insight into that now?

Janet Woodcock: This is Janet Woodcock. Once we nail down the identity, we'll be able to distinguish because there are certainly Heparin-like molecules in other risk GAGs that are part of the (unintelligible) by-product of the production process and so that was why that was one possibility.

But there's also the possibility this was intentionally added and with our analytical work, we're going to be able to determine, I hope, whether or not these look like natural molecules or whether these look like molecules that have had some synthetic alternation and of course, that would point us in different directions and that's still ongoing. Dr. Nasr, do you have any other comment?

Moheb Nasr: No, I think you descried it very well, but this is a valid question and this is (unintelligible) to our laboratory and scientific investigation is that to find what it is and how it got there.

Julie Zawisza: For clarification, did you say the Heparin-like molecule is a gag or gagged?

Janet Woodcock: Gag.

((Crosstalk))

Julie Zawisza: What is a gag?

Janet Woodcock: Glycosaminoglycan, okay?

Julie Zawisza: Glycosaminoglycan

Janet Woodcock: And I'm sure that's enlightened everyone on the call. But these are Heparin-like molecules. Heparin is also one of these, but there's a whole family of them, and what we're trying to do is distinguish amongst them, but there's difference in this chemical or that chemical. It's like very close relative, and we're trying to tell whether you know, they're twins almost, and is it this twin or that twin.

Julie Zawisza: Thank you. I'll look that up on Wikapedia.

Coordinator: Our next question comes from Chris Hollis with FDA News. Your line is open.

Chris Hollis: Hi, good afternoon. I have a question on the MOU with China, the Memorandum of Understanding. Can the FDA speak to how the Agency is working with the Chinese government on this and how maybe that is putting the Memorandum of Understanding to a test/

Julie Zawisza: Memoranda of Agreement?

Chris Hollis: Yeah, yeah.

Julie Zawisza: Fortunately we have Walter Batts here who is from our Officer of International Programs, so we'll ask him to address that.

Chris Hollis: Okay, great.

Walter Batts: Yes, the MOAs have come into play here in a couple of aspects of this. First when we identified this concern and felt the need to travel to China to do inspections, we got the support of the Chinese government to facilitate the travel over there fairly quickly.

We were joined in the facilities by representatives from the Chinese State Food and Drug Administration and we continue to have conversations with them as they are doing their testing and staying in communication so that any findings that they have, they will share with us and vice versa.

Julie Zawisza: Thank you. Operator, how many more people are in the queue?

Coordinator: It looks like we have about five or six still holding.

Julie Zawisza: I don't think we can take that many. Let's try one or two and we'll see how we do.

Coordinator: Okay. Our next question will come from Susan Heavey with Reuters. Your line is open.

Susan Heavey: Hi, thanks for taking my call. I know you said you can't name the five manufacturers who have made commitments, but can you give us a number of how many have not made commitments?

Steve Silverman: No, I can't actually. It's not that I'm trying to be coy. This is Steve Silverman again. What you're asking basically is for us to define the universe of firms that might want to bring this product into the country and then subtract five from it and it's not a calculation I'm able to make sitting here.

Susan Heavey: Okay. I don’t know who could answer but they spoke earlier, but when is the (unintelligible) planning on starting their test – the next few days or week?

Julie Zawisza: Dr. Nasr?

Moheb Nasr: Can you repeat the question please?

Susan Heavey: You mentioned that you were working with Japanese officials to start testing over there. When is that set to begin?

Moheb Nasr: I think the testing is currently happening.

Susan Heavey: Okay.

Julie Zawisza: Thank you; next question, please.

Coordinator: Our next question comes from Tom Burton with the Wall Street Journal.

Julie Zawisza: Hi, Tom.

Coordinator: Your line is open, sir.

Julie Zawisza: Go ahead, Tom.

Tom Burton: Hi, I'm just returning quickly to a question that was asked before, but didn’t seem to me was adequately answered and that is whether the FDA intends to inspect these workshops or factories or not and if not, whether the Chinese will and when.

Julie Zawisza: Okay, we’ll try it again.

Rick Friedman: We are in discussions with the Chinese government on multiple follow-up measures and further follow-up at these relevant sites is definitely something that's been discussed with them.

Tom Burton: Who was speaking there?

Julie Zawisza: That was Rick Friedman.

Tom Burton: Oh, thanks.

Julie Zawisza: Thanks, Tom. Next question please.

Coordinator: Our next question comes from Nancy Faigen with Scrip Pharma News.

Nancy Faigen: Yeah, this relates a little bit to that previous question. Are there any API (unintelligible) that comes from pigs in the US and what is the role of the USDA?

Steve Silverman: The answer is yes. In fact, North America, both Canada and the United States, pigs are used in source materials, starting materials for the production of Heparin and the USDA and I could say Canada also because I've seen some of their standards recently, and they require that healthy pigs are used for the production of the starting materials for Heparin, both countries, Canada and the US.

Nancy Faigen: Would the USDA have any information on standards? How would one find out about those standards?

Steve Silverman: I know the USDA Web site has some great stuff on BSE and other standards for animals and animal health, so I would refer you to the Web site. There is some very good material on there.

Nancy Faigen: Oh, thank you.

Julie Zawisza: And I would, this is (Julie), refer you to their press office because they would be able to point you to the right people and the right materials.

Julie Zawisza: With that, ladies and gentlemen, we're going to conclude this briefing this afternoon. I'd like to thank Dr. Woodcock and our half a dozen speakers here, Steve Silverman, Domenic Veneziano, Ann McMann, Moheb Naxr, Rick Friedman and Walter Batts, and I'd like to thank all of you for joining us today.

We have the briefing available on instant replay in about an hour. If you have a media advisory, you'll have those phone numbers, but I'll say them quickly, 866-463-4970. And for international callers, 203-369-1405. If you have follow-up, please call the press office here. You have that number and again, I invite you to check our Web site for updates.

We do have a Heparin Web site with the graphics and other information. As you know, as this issue continues to evolve, it's very dynamic. If anything would happen, today, tomorrow or the next day, we'll keep you informed, but you should still keep checking the Web site looking for emails from us, and we promise you that we will give you regular updates. Thanks again and have a very pleasant afternoon and have a great weekend.

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

END