FDA MEDIA BRIEFING ON HEPARIN

Moderator: Julie Zawisza
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3 p.m. EST

Coordinator: Welcome and thank you for standing by. At this time all participants will be in a listen-only mode. After the presentation we will have a question and answer session. To ask a question at that time press Star 1 on your touchtone phone. Today's call is being recorded. If you have any objections you may disconnect at this time.

Now I'd like to turn the meeting over to Ms. Julie Zawisza. Ma'am, you may begin.

Julie Zawisza: Thank you, (Janice). Ladies and gentlemen, I am Julie Zawisza, the Assistant Commissioner for Public Affairs with FDA. And I'd like to thank you all for joining us. And thank you for your patience this afternoon.

We want to update you on the latest information we have on our heparin investigation.

And our speaker this afternoon is Dr. Janet Woodcock, who is our deputy commissioner for scientific and medical programs. Also, our Chief Medical Officer. And also the Acting Director of the FDA Center for Drug Evaluation and Research.

After Dr. Woodcock makes her remarks, then we will open the line to your questions. Dr. Woodcock.

Janet Woodcock: Thank you, Julie. We are here to discuss some global developments involving the blood thinning drug, heparin.

As all of you know, Baxter Healthcare Corporation recalled all its single-dose, multi-dose, and HepLOCK heparin flush products on February 28th, because some patients were experiencing serious allergic reactions or hypotension after receiving a “bolus” dose of the drug.

Yesterday we reported finding that some of the heparin products and heparin active pharmaceutical ingredient manufactured by Baxter’s supplier, Scientific Protein Laboratories, were contaminated by a heparin-like substance.

Today we were notified by the German drug regulatory authorities that they have recalled heparin manufactured by a German company after learning about adverse events that fit the profile of the adverse events we have seen with heparin products here in the United States.

The German authorities have identified a cluster of events at a dialysis center. They also have other reports where they don't have the specific manufacturer, but they also have another - a cluster of similar reports from doctors.

What is significant about the German recall is that the heparin active ingredient in that product was not obtained from SPL like the Baxter product. Instead, it was obtained from another API supplier entirely.

Yesterday we promised to release test methods that manufacturers and global regulators could use to determine whether their product is contaminated with this heparin-like substance that is not heparin.

We are now posting these tests. One test is called capillary electrophoresis. And the other is nuclear magnetic resonance spectroscopy.

Use of these tests makes it possible to identify specific results or signals that should not be seen in heparin. Now we can talk more about the technical details of these tests in the Q&A, but basically what you would see in these tests is, for example, to use a very simple analogy, if some substance, you would shine a light on it and it came back green, you would look at the Spectrum and you would say that is a green result. This is looking where we get a signal say red or purple that shouldn't be coming back from that substance.

I am sorry if I am simplifying, but that is basically what we are talking about here. It doesn't definitively identify the ingredient - the contaminant, but it is a signal that should not be seen in heparin.

Given the announcement by the German authorities, we thought it was important to post these tests on-line as soon as possible. We are requesting that all API and finished product heparin manufacturers evaluate their products using these tests. And companies should call FDA with any positive test results and we will be posting a telephone number and an e-mail address on our website, along with the test.

Before opening to calls, we would also like to point out that SPL announced late yesterday it was recalling its heparin API that tested positive for contamination.

So that is the information we would like to relay. And I am sure you have questions. And we will open up the floor for questions. Julie.

Julie Zawisza: Thank you, Dr. Woodcock.

Before we open to questions, I would like to introduce a few technical experts from FDA who are on the phone who will assist Dr. Woodcock.

(Deb Autor), who is the director of the Office of Compliance and FDA Center for Drug Evaluation and Research, is joined by Michael Rogers, who is the director of the Division of Field Investigations in FDA's Office of Regulatory Affairs. And Dr. Moheb Nasr, who is the director of the Office of New Drug Quality and Assessments in the Center for Drug Evaluation and Research.

So let's go ahead and open up the line to callers. And I would ask you to please state your name and affiliation. And we will take one call - one question and one follow-up.

Coordinator: If you would like to ask a question, press Star then 1.

Our first question comes from Peggy Peck, from Medpage Today.

Peggy Peck: Yes. Thank you for taking our questions.

I'm - about the German announcement, can you tell us where the - where did the crude Heparin product come from - that the German manufacturer was using? What country?

Janet Woodcock: The German regulatory authorities are still pursuing their investigation. And we would refer you to them. We are going to remain in contact with them as they go through evaluating the situation.

Peggy Peck: So, and on follow, did they use the same tests that - the capillary electrophoresis, and the MRI spectroscopy to identify the problem? Or have - I guess they haven't identified. They have just reported - they have just reported events. Is that correct?

Janet Woodcock: Yes, they have a fairly, you know, they have a fairly large cluster of serious adverse events, such as anaphylaxis and shock and so forth that has caused them to initiate this recall.

Also, just a clarification, it is not MRI, it is NMR....

Peggy Peck: NMR, I apologize. OK.

Janet Woodcock: Next question, please.

Coordinator: Our next question is from Donna Young, from Bioworld Today.

Donna Young: Hi. Thank you for taking my question. I - first of all, I just want to clarify the contaminant itself. You still have not linked the contaminant to the allergic reactions. Is that correct?

Janet Woodcock: Yes. What we have found is that in the U.S., the batches we have tested that have been implicated in the allergic reactions - the cluster of allergic reaction have had this contaminant in.

Other batches, say from previously, or from manufacturers who have not been implicated in these allergic reactions, have not had the contaminant.

But we haven't found a causal link between the contaminant and the allergic reactions. And there could be something else in there that was actually causing the allergic reactions.

Donna Young: Okay. And then my follow-up question is, as far as - since now it has been found in Germany, do you have concerns that this particular contaminant could show up in other drugs? Like, is this particular API used in other drugs other than heparin? If so, is there some chance that this contaminant could show up in other drugs?

Or is there a possibility that it is being used as some kind of filler that could potentially show up in other drug products?

Janet Woodcock: No, this is - this particular API is heparin. And the contaminant was able to get through the process, so to speak, because it mimics heparin in the tests.

So mist small molecule APIs for example that would not at all be the case. So I don't think we have a global concern about this contaminant in other drugs. We are concerned about worldwide this contaminant in heparin and making sure it stays out of the helprin supply.

Donna Young: Thank you.

Julie Zawisza: Let's take the next question.

Coordinator: Our next question is from Lauran Neergaard with Associated Press.

Lauran Neergaard: I am trying to follow up on who exactly you want to do this testing now? Have you all assured yourself that all of the heparin remaining on the U.S. market is free of the contaminant?

Have you told - I guess it is just APP that is still the only remaining supplier to regularly use the test. How do you want it to be used?

Janet Woodcock: Certainly some of the APP heparin has been tested. There are many different types of heparin on the U.S. market for IV flushes and for other uses.

We would like all manufacturers of heparin and - to test their heparin products, as well as their APIs to make sure this contaminant is not in there. From the smaller volume uses where we did not see these adverse events, to the large mass use of heparin - the bolus use of heparin intravenously.

So we would like all manufacturers to be testing their heparin with these tests.

Lauran Neergaard: Okay. So before when we were talking about heparin supply and APP versus Baxter, we were just really talking about those bolus doses?

Janet Woodcock: Yes.

Lauran Neergaard: There is truly a lot of manufacturers out there?

Janet Woodcock: There are many more manufacturers for the smaller uses of heparin - where there is a smaller amount of heparin. It is added to various things. It is in IV flush solutions and so forth.

Lauran Neergaard: Okay.

Julie Zawisza: Thank you. Next question.

Coordinator: Our next question is from Walt Bogdanich with the New York Times.

Janet Woodcock: Hi Walt.

Walt Bogdanich: Hi. Do you know the answer to the question about where the crude heparin came from that has been implicated in the Germany situation? I mean, do you know the answer to that question?

Janet Woodcock: What the German authorities told us is, they have tracked some of it back. But they don't know the manufacturer of many of the events that have been reported.

The majority of the events have been reported to them actually, they do not have the manufacturer's name. And they are working on getting that.

Walt Bogdanich: Okay. How about if we say country? Did they come from China? Did they ever mention the word China?

Julie Zawisza: I think you would have to call the German authorities.

Walt Bogdanich: No. But I am asking you.

Julie Zawisza: Yeah, we would refer you to the German authorities on....

Walt Bogdanich: Do you know the answer to that question?

Julie Zawisza: Our discussions with other regulatory authorities sometimes have to be held confidential. But we could refer you back to them - to the German regulatory agency.

Walt Bogdanich: Yeah, can I - could you answer yes or No? I mean, you are not revealing anything. I am just asking, do you know the answer to that question?

Julie Zawisza: Yeah, it is still evolving.

Walt Bogdanich: You're not going to answer my question! I will move on. Go ahead.

Julie Zawisza: (Unintelligible) to be definitive when we are in an active investigation and the data is changing regularly. We are not trying to be (unintelligible) helpful here.

Walt Bogdanich: Okay.

Julie Zawisza: Do you have anything else, Walt.

Walt Bogdanich: No.

Julie Zawisza: Okay. Thank you. Next caller.

Coordinator: Our next caller is from John Wilkerson, from FDA Week.

John Wilkerson: Yet, is this heparin case an example of the difficulty in predicting how minor changes to the manufacturer of a biologic can change its risk profile?

Janet Woodcock: We do not know how this contaminant was introduced into the product. Whether it was changed in the biological source material, change in the processing, or it was deliberately introduced.

John Wilkerson: And then, so how do you guard against this in the future? Should the specifications that USP sets be tighter for APIs?

Janet Woodcock: Well, I think that is a blanket question. What we are focusing on here is the testing that we would do to keep this particular contaminant out of the heparin supply.

We will certainly evaluate. And going forward, when we are done with this investigation, the acceptance criteria for heparin API.

John Wilkerson: Thank you.

Julie Zawisza: Next question, please.

Coordinator: Our next question is from Bruce Japsen, from the Chicago Tribune.

Janet Woodcock: Hi, (Bruce).

Bruce Janson: Yeah, good afternoon. It is Bruce Japsen.

You know, I would like to follow-up on Mr. Bogdanich's question. How can you assure the American people here that this is not something that has entered the U.S. supply. And if there are concerns about heparin coming from China, I mean, why will you not disclose what it is you know thus far, given the fact that people are concerned here?

I mean, this is now an international situation potentially. I mean, is the company from the U.S.? You know, there are a lot of questions here.

You know, and we are trying to help you answer the questions and get the word out, and you are not giving us anything.

Julie Zawisza: Okay, we do not have any information this is a U.S. company involved in Germany.

Bruce Japsen: Yeah, I am sorry?

Julie Zawisza: It was not a U.S. source involved in Germany.

Bruce Japsen: Does the company have any business? I mean, how do we know - we don't even know where this heparin, that Baxter used, where it came from. And, you know, we are trying to figure all that out. Do you know what I am saying?

I mean, how do we know that this - if there are so many heparin suppliers, do you know for sure that this company does not bring crude heparin into the United States through various channels?

Julie Zawisza: Michael Rogers, are you on the line?

Deb Autor: This is Deb Autor. I can address that a little bit.

We just found this information out today. We are obviously working as quickly as possible to analyze any potential impact on U.S. market or worldwide.

And the most important thing we think is to get the screening methodology out there, so that companies are able to test heparin for themselves, to make sure their heparin is safe. Since we don't know the scope of the problem, that is the best thing we can do.

Julie Zawisza: Anything else, Bruce.

Bruce Japsen: Well, yeah actually there is. I mean, so you don't know the scope of the problem. You are getting out the testing thing. But I am telling you what, if I am a hospital in the United States, or a dialysis center, I want to know what - I want to know what product to look out for.

Janet Woodcock: (Unintelligible) know that too. We…

Bruce Japsen: I mean, should we be looking out (unintelligible) are you going to tell - are you telling the United States hospitals and dialysis centers to test every heparin product there is that is coming in right now?

Janet Woodcock: We are telling the manufacturers. There have been tests done on the APP product that they used in dialysis centers and in cardiac surgery. And that has shown no contaminant.

We are monitoring for adverse events to insure that there hasn't been a raise in adverse events in the U.S. And with this testing method, there will be a way to protect the heparin supply, because all the various manufacturers can test their product.

We are not asking hospitals, or suggesting hospitals that they test product.

Coordinator: Our next question is from Lynne Peterson, of Trends in Medicine.

Lynne Peterson: Thank you. Yesterday, one of the FDA press people told me that there are other tests that you are using for identifying this, other than capillary electrophoresis and nuclear magnetic spectroscopy, but declined to tell what those tests were.

Could you tell us those tests now?

Janet Woodcock: There is a very wide variety of tests that are being done in research laboratories that specialize in these type of Glycosaminoglycans, alright. And they aren't applicable to screening products, alright.

These are investigations that are going on to try to find out what exactly this contaminant is.

So these are - these two tests that we are releasing are the appropriate tests. They are more complicated than most quality control - average quality control labs would use, but they are certainly within the scope of university laboratories and pharmaceutical laboratories to conduct. So these are tests that would be appropriate to use as screening.

Lynne Peterson: Are they all that are needed to detect this? Or in order to initially detect and determine this heparin-like contaminant, would you need something else?

Janet Woodcock: No. We believe these tests would be the best test to rule out the presence of a contaminant in the heparin.

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

Coordinator: The next question is from Ricardo Alonso-Zaldivar with the Los Angeles Times.

Janet Woodcock: Go ahead, Ricardo.

Ricardo Alonso-Zaldivar: Hi. Thanks for taking my question. I just want to get a better sense of the testing that you are calling for. And can you say again? Is it a

requirement that the manufacturers test their product with these more sophisticated tests?

And can you give us a more precise sense of, you know, how many manufacturers? What the scope of this (unintelligible) - of this step you are taking is?

Julie Zawisza: Dr. Nasr, could you take the question on the methodology?

Moheb Nasr: Yes. This is Moheb Nasr. We have currently in place regulatory requirements of testing for API - for heparin API.

These two tests are in addition to the existing regulatory requirements.

Ricardo Alonso-Zaldivar: Okay. And can you give us a sense of how many manufacturers are going to be affected by this? And, you know, kind of like the breadth of it? Is it something that is very broad or relatively narrow? You are talking to lay people here.

Moheb Nasr: It is - yes, it is relatively narrow number of companies who would need to do that test.

Ricardo Alonso-Zaldivar: Okay, well relatively narrow? Fewer than 10? You know, some better idea.

Moheb Nasr: I would think most likely fewer than 10, but I would defer to Deb Autor or Mike Rogers to provide more specific information.

Ricardo Alonso-Zaldivar: Can you guys follow up with that?

Julie Zawisza: Deb, do you have a number or do we need to get back to Ricardo?

(Deb Otter): I think we should get back to him.

Julie Zawisza: Okay. Thank you.

Ricardo Alonso-Zaldivar: Thank you.

Julie Zawisza: Anything else, Ricardo.

Ricardo Alonso-Zaldivar: Any more information on what the contaminant might be?

Moheb Nasr: This is Moheb Nasr. Not at this time. We are currently doing a very extensive investigation at our level (unintelligible) and the leading academic institutes in the U.S.. But we do not have the identity of this contaminant at this time.

Julie Zawisza: Okay. Thanks. Let’s go to the next question.

Coordinator: Our next question is from Kim Dixon with Reuters.

Kim Dixon: Hi. Thanks. Can you - are you able to quantify the number of adverse reactions seen in Germany and/or whether there were any fatalities?

And do you have any sense as to who suppliers - I guess, maybe this is a reiteration, but who supplies the European market? Is there a big Baxter-type company, you know that’s the major player?

Janet Woodcock: I can't answer the European market. The German authorities told us they do not expect any shortage as a result of this recall.

They also said there were - they had no reports of fatalities.

Kim Dixon: No fatalities. And what about any estimate on the number of deaths?

Janet Woodcock: That would be fatalities.

Kim Dixon: I'm sorry. I met adverse events.

Janet Woodcock: Yeah, they had fewer than 100 reports.

Kim Dixon: Okay. And then maybe just one follow up. What about - are you - how much heparin did they recall in Germany?

Janet Woodcock: We don't have that information.

Kim Dixon: Okay. And then maybe one final question.

You said other heparin - You said there were some other smaller companies in the U.S. that make different versions of heparin to be used in smaller amounts. Is that the fewer than 10 companies that we were talking about in the last question?

Janet Woodcock: Yes. We were talking about the whole scope of companies. We will probably have to get back to people with the exact - the information to the extent we can on how many different companies would be involved.

Kim Dixon: Okay.

Julie Zawisza: Let’s move on.

Kim Dixon: Thank you.

Julie Zawisza: (Unintelligible) two questions please. We have a lot of questioners. Next question.

Coordinator: Our next question is from Tom Burton with The Wall Street Journal.

(Tom Burton): Can you tell us please what the name of the German company is? The API supplier? Where these incidents took place? And who at the German drug agency can give us further details?

Janet Woodcock: The name of the Company - the brand name is Heparin Rotex Medica.

Tom Burton: Spell that please.

Janet Woodcock: R-O-T-E-X, M-E-D-I-C-A.

Tom Burton: And who makes it?

Janet Woodcock: I think that's who makes it.

Tom Burton: You think, or you know? Is that the company?

Janet Woodcock: Deb?

Deb Autor: Yeah, that's the name of the finished product manufacturer that I have (unintelligible) Heparin Rotex Medica.

Tom Burton: Okay. And you indicated you don't know the name or the source of the API?

Janet Woodcock: Well, what we have said is that we have to refer you to the German authorities for that kind of information.

Tom Burton: Right. But do you know?

Julie Zawisza: We already went over this. We are going to refer you to the German authorities. As soon as we have more information, we will release it.

Tom Burton: And what's the number of the adverse events?

Janet Woodcock: It is fewer than 100. But many of them, they can't trace the particular manufacturer - we were told, because of the way the reports were done. They simply have reports.

Tom Burton: And in what German city, and what dialysis center?

Janet Woodcock: Well, we don't have - we just received what's called a rapid alert from them about this recall. We don't have an extremely comprehensive report from them.

Tom Burton: Okay. And what's the full name of the German drug agency? And whom could we reach there for further details?

Janet Woodcock: The Paul Ehrlich Institute.

Julie Zawisza: No. It's the (Bundus) Institute for A-R-Z-N-E-I. M-I-T-T-E-L medicine product. B (unintelligible) FARMA.

Tom Burton: Spell the second word. (Bundus) Institute for what?

Julie Zawisza: Arzei Mittel.

Tom Burton: Can you spell it please?

Julie Zawisza: A-R-Z-E-I, M-I-T-T-E-L, (unintelligible) Medicine Product - M-E-D-I-Z-I-N, P-R-O-D-U-K-T-E.

Julie Zawisza: Also known as BFARM. That's their abbreviation of their agency.

Deb Autor: While we are spelling out German words. Let me also correct name of the manufacturer. The product that I mentioned is Heparin- Rotex Medica. The manufacturer is Rotex Medica R-O-T-E-X, M-E-D-I-C-A GmBH. So G-m-b-H. And the last word is Arzen Mittelwerk, I believe - A-R-Z-N-E-I M-I-T-T-E-L-W-E-R-K.

I will do that one more time. Rotex Medica R-O-T-E-X, M-E-D-I-C-A. That's one word. GmBH is the second word with a Capital H at the end. And the last word is A-R-Z-N-E-I M-I-T-T-E-L-W-E-R-K.

Julie Zawisza: Thanks, Deb. Let's move on to the next question.

Coordinator: Offered next question is from Elizabeth Weise with USA Today.

Julie Zawisza: Go ahead, Elizabeth.

Elizabeth Weise: Hi. Thanks for taking my call.

Do you guys know - you don't know the exact place where these incidents took place? Do you have even a sense of the country so we can go check the

newspapers there? South, north? There's a lot of newspapers in Germany. I don't want to have to read them all.

Julie Zawisza: Yes. No. Sorry, we do not know - we do not have that level of information. As I said, we just received this alert.

Elizabeth Weise: What time did it come in?

Julie Zawisza: This morning.

Elizabeth Weise: This morning. Okay. Thank you.

Julie Zawisza: Okay. Thank you. Next question.

Coordinator: Our next question is from Jyllian Kemsley with Chemical and Engineering News.

Jyllian Kemsley: Hi. Thank you. I just wanted to clarify two things.

One is, have the German authorities tested the - either that heparin products or the API to look for the contaminant you have identified?

Julie Zawisza: Our understanding is no. They simply identified adverse events.

Jyllian Kemsley: Okay. And the other one is that, you said the new testing looking for the contaminant will be a way to protect the heparin supply.

Now, previously I understood that the this has been identified in lots associated with the adverse reactions. So there was a correlation, but not a

direct causal link. Do you now believe there is a direct causal link between the contaminant and the adverse reactions?

Julie Zawisza: No. As I said, we have an association here. (Unintelligible) in general, prior lots of heparin over the years have not contained this contaminant - have not been associated with this set of adverse reactions. So we don't have a mechanistic causal link.

Jyllian Kemsley: Okay. Thank you.

Julie Zawisza: Next question.

Coordinator: Our next question is from Daniel Poppy of Pharmasia News.

Daniel Poppy: Hi. Thanks. Do you have a sense of how many non APP heparin products are being used, compared to the APP products in the U.S.?

Julie Zawisza: Again, I think we will have to get back to you on that.

Daniel Poppy: Okay. Thanks.

Janet Woodcock: We do have a sense, because we have gone through with our drug shortage team and evaluated all this to make sure there will be no shortages. But I - we don’t have the numbers in hand.

Daniel Poppy: I mean, I know you mentioned 10 manufacturers. But not a sense of the amount out there.

Janet Woodcock: Deb, are we still looking at that?

Deb Autor: Yeah. I mean, the - yes, we are still looking at that. The - many of the other manufacturers are making small - very small mass or volumes of heparin that weren't implicated in these reactions.

Daniel Poppy: Okay. Thanks.

Julie Zawisza: Send an e-mail to Karen Riley so that she can get that information back to you. Next question please.

Coordinator: Our next question is from John Rockoff of The Baltimore Sun.

John Rockoff: Thanks. Are you going to be providing any technical assistance, or sending folks to Germany at all?

Julie Zawisza: We have already provided them assistance. And, you know, we will be talking to them. I don't think - I don't think they - the Germans really invented analytical chemistry. So....

John Rockoff: So what sort of help did you provide? Just sort of…?

Julie Zawisza: We talked about our test methodologies and so forth that we are posting. And, you know, provided them - and what we know about the contaminant - what kind of chemical it is.

John Rockoff: Lastly, do you - you don't have like a contact name or number, or e-mail, for the German Drug Agency, do you?

Julie Zawisza: No. I'm sorry.

John Rockoff: Thanks.

Julie Zawisza: And we have time for one more question.

Coordinator: Our next question is from Jennifer Corbett with Dow Jones.

Jennifer Corbett: Thanks. My questions have been answered already.

Julie Zawisza: Okay. Thank you. Ladies and gentlemen, this concludes our call.

And I would like to assure you that as we get more information, we would like to share it with you. These are very complicated issues we are talking about, and we don't have all the answers yet.

Despite that, we want to be able to talk with you as we go along. Your questions are very good. We are asking the same questions of our - in our investigation at this time.

So appreciate that (unintelligible) when we have those answers, we will get them to you.

I would like to thank our speakers, Dr. Janet Woodcock, and then also Dr. Nasr and Deb Autor for your assistance today. Thanks to all of you on the phone.

And we have a replay of this call that should be available in two hours or so, you should have that replay number. I don't have it in for me. Yes, I do. One moment.

The replay number is 866-414-6081 if you are in the United States. If you are overseas, 203-369-0680. And if you will check our Web site later this

afternoon, we will have the test method that Dr. Woodcock described posted probably in the next hour or so.

And I would like you to stay tuned this week and next week. If we have new information, we will hold another briefing. We will have regular updates until these matters are resolved.

Thanks again. Have a good afternoon.

Coordinator: Today's call has ended. You may disconnect at this time.

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