FDA MEDIA BRIEFING ON HEPARIN

Moderator: Julie Zawisza
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Julie Zawisza: And at this moment I'd like to turn it over to Dr. von Eschenbach.

Andrew von Eschenbach: Thank you Julie and first of all let me thank all of you for joining us at FDA today. This is a call that is part of our committed effort to keep you informed of developments as they occur and issues that are important to the American public.

And I know at present we have all been engaged in an intensive effort to address the adverse events reported with the use of heparin and it's an area of great concern and interest to you.

So we wanted to bring you up to date on some of our efforts and some of our most recent findings in that regard. But it's important to just let me put this in context.

As we are putting the welfare of patients and the people we serve first and foremost, we've been placing greater emphasis on open and frequent communication.

But there are three important facts I really want to emphasize at the beginning. One, this is a part of an ongoing methodical comprehensive investigation of a very complex story.

It’s a complex clinical setting in which these adverse events occurred, it’s a complex drug and it’s complex particularly with regard to its production and distribution.

And I know that you would like the whole story, but what we are giving you are the pieces that are developing as we develop them and helping you understand the progress that we’re making in terms of really identifying and understanding the source and the core of the problem and the adverse events.

And particularly what we’re doing to mitigate and resolve those issues and those and those concerns. I really want to emphasize at the outset the high degree of cooperation and collaboration that’s occurred on the part of many parties.

That’s not just simply the high degree of collaboration and coordination which occurred across the Food and Drug Administration from our field activities, our international program effort and certainly the efforts that have occurred in CDER, the Center for Drug Evaluation and Research.

But there also has been a high degree of collaboration and cooperation on the part of other federal agencies like CDC, federal and private laboratories, especially some in academia.

A high degree of collaboration and cooperation on the part of Baxter, the company that’s involved, and I want to emphasize certainly the high degree of collaboration and cooperation we’ve received from our counterparts in China.

And as FDA embarks upon the effort to engage in China and is part of our comprehensive investigation, our recent memorandum of agreement with

China has certainly facilitated our opportunity to really effectively address the concerns there at the source of production.

There have been a number of important steps that have been taken that have been able to protect the American people as we have gone forward. And I want to emphasize the importance of them.

As we are carrying out this investigation, we're carrying it out in the context of multiple interventions on our part, on the part of the company with regard to the whole - and the cooperation that we've received that I believe really has helped to secure and mitigate any current concerns with regard to the use of this product in patients but we're paying very, very close attention to that.

You've been briefed already in many aspects of this effort. And so at this point what I want to do is turn the briefing over to Dr. Janet Woodcock, who is the acting director of CDER, who is going to bring you up to date on very recent findings as a part of our investigation.

Some the implications of those findings and the steps that were taken to further continue this investigation and this assessment, and then we'll be open to your questions in Q&A. Janet?

Janet Woodcock: Thank you Dr. von Eschenbach. We're here to provide you with an update on FDA's ongoing investigation into adverse events associated with Baxter Healthcare Corporation blood thinning drug known as Heparin.

In early February after learning about a spike in adverse events involving this product, FDA launched a far ranging investigation both in the US and abroad.

This included inspecting Baxter's domestic facility, examining Heparin product in the US and sending a team of experts to China to conduct a comprehensive inspection of the Changzhou SPL facility that makes the active ingredient for this drug.

While the FDA has not determined the root cause of the adverse events that were observed, we have found a heparin-like compound that is not heparin present in some of the active pharmaceutical ingredients or APIs produced by Scientific Protein Laboratories, which maintains a facility in Wisconsin in addition to the Changzhou plant.

This contaminant is present in significant quantities in some of the APIs, accounting for approximately 5 % to 20% of the mass of the substance tested depending on the sample.

It reacts like heparin in some of the tests, the conventional tests that are used for heparin, which is why conventional release tests, or acceptance tests of ingredients might not detect this contaminant.

At this point we do not know how the heparin-like compound got into the heparin active pharmaceutical ingredient, but we are continuing to aggressively investigate this.

We don't yet have a direct causal link between the contaminant and the adverse events. We know that some of the suspect batches of heparin that were causing the adverse event have this contaminant in it.

So there is an association between the contaminant and the presence of adverse events, but it is not a direct causal link at this time.

In addition we don't know if any other heparin products used worldwide, outside the U.S., might contain this contaminant and that's something that we're gong to be looking in to.

To ensure that all is being done to provide a safe supply of heparin, later this week we will release recommendations on how manufacturers and regulators worldwide can screen for this contaminant.

We will be releasing some specific testing procedures. Today the manufacturer APP supplies single and multiple dose vials of heparin in the United States. Tests done on that source of the drug do not show contamination.

Fortunately it can provide an adequate supply of heparin vials in the US market and FDA intends to continue to monitor the availability of heparin and work with manufacturers so that they can continue to meet the demand.

FDA and Baxter are continuing to receive and analyze adverse events related to heparin. I want to emphasize FDA wants to warn healthcare practitioners not to use any Baxter heparin that they might have that has been recalled, which includes single-dose and multi-dose vials and Hep-Lock, heparin flush products from Baxter.

We are having information emerge literally every hour almost on this situation and we will provide the public with further updates as we learn more about this contaminant.

Julie Zawisza: Thank you Dr. Woodcock and Dr. Von Eschenbach, thank you for your previous remarks. Ladies and gentlemen, before we start the question and

answer session I'd like to introduce three other FDA officials who are sitting around the table with us.

These are people with technical expertise who may be assisting Dr. Woodcock on some of your questions.

We have Dr. Moheb Nasr, who is the director of the office of New Drug Quality and Assessment in our Center for Drug Evaluation and Research, Deborah Autor who is the director of the Office of Compliance in FDA's Center for Drug Evaluation and Research, and Michael Rogers, who is the director of the division of field investigations at FDA's Office of Regulatory Affairs.

Now I want to remind you that this briefing is for credentialed media and we have a lot of people on the phone, which is good. But I'd like to ask you to limit yourselves to one question and one follow up and also please state your name and affiliation.

(Barbara), we're ready for the first question.

Coordinator: Our first question comes from Elizabeth Weise with USA today.

Julie Zawisza: Hi Elizabeth.

Elizabeth Weise: Hey, thanks for taking my call. So in these samples which you found the 5% to 20% of the substance tested, how did you find that there was a contaminant there?

Janet Woodcock: We've been doing more advanced laboratory testing both in FDA laboratories and with a multitude of academic collaborators, and Baxter has also been

doing testing and we have been sharing scientific information and multiple test methods and scientific laboratories just recently came to this conclusion.

Andrew von Eschenbach: For example I mean one of those sophisticated techniques was the use of nuclear magnetic resonant to be able to determine a difference between this particular lot of heparin as compared to others.

And so as Dr. Woodcock's pointing out, we've gone beyond the realm of what is standard and usual to highly sophisticated kinds of testing to identify a difference and then track that difference to what that specific adulterant is.

Julie Zawisza: That was Dr. von Eschenbach. Now does that do it for you?

Elizabeth Weise: Yes it does, thanks.

Julie Zawisza: Great, thank you. Next question please.

Coordinator: Your next question comes from Gardiner Harris with New York Times.

Julie Zawisza: Hi Gardiner.

Gardiner Harris: Hi, thanks so much for taking my question. Can you - so it sounds like these tests were all done in the United States, can you tell us…

Julie Zawisza: Gardiner could you speak loudly - more loudly?

Gardiner Harris: Yes, I'm sorry.

Julie Zawisza: (Unintelligible) or rather. Thank you, perfect.

Gardiner Harris: It sounds like your tests were done in the United States, can you describe a little bit in more detail what the adulterant is. This sounds like this fake heparin, and can you tell us anything that you have learned from your inspections from China about how you think this got into the heparin.

Was somebody just trying to fool you, was this just basic fraud? Do you know?

Janet Woodcock: At this point we do not know whether the introduction of the contaminant was accidental as part of the processing or biological process or it was deliberate.

We do not know and we have no further information on that.

Gardiner Harris: Can you tell us anything about what the adulterant is, I mean is this just - I mean how it might be made, is this just a different form of pig intestines or this is this something completely different?

Janet Woodcock: There are similar - there are other glycans in pig intestine but we do not have a final identification of the compound, it is a - similar to heparin glycan and we are in the midst of doing very advanced analytical work to determine the exact identity of it.

Gardiner Harris: So I'm sorry, I was just - I'm just stupid about what a glycan is, what is the glycan, does that mean that…

Janet Woodcock: I'll turn it over to Dr. Moheb Nasr.

Moheb Nasr: Glycans are complex polysaccharides. It's a group of chemicals that are complex polysaccharides. So the suspect material is related to these polysaccharides.

Janet Woodcock: And heparin is a complex polysaccharide as well. And so these are very - from the layman's point of view-- they are big complicated molecules I think and that's so part of the difficulty.

Gardiner Harris: And this stuff would also be coming from pigs then, the fake stuff as well, is that what you're saying?

Janet Woodcock: Will you say that again please?

Gardiner Harris: I'm sorry, I'm sorry to take up so much time, it's just - so the fake stuff is also coming from pigs but from a different process of pigs? Or it is coming from something completely different, or do you not know?

Janet Woodcock: We do not know.

Gardiner Harris: Thanks.

Julie Zawisza: Thank you, next question please?

Coordinator: And as a reminder, to ask a question press star 1. And our next question comes from David Greising from the Chicago Tribune.

Julie Zawisza: Hi David.

David Greising: Hello, and thanks for putting this call together. I wanted to ask Dr. (Eschenbach) about some of the conflicting information that has come out of the FDA about your - the scope of your ability to inspect Chinese plants based on some information that has come out.

It appears the FDA over the last five years or so has inspected about 15 plants in China on average. There are more than 700 plants producing API and finished drug products.

And yet FDA has claimed at times at least that it has inspected every one except for this one plant, although your own national science board study said that it wouldn't be possible for FDA to do so.

So can you clear up once and for all this question of whether FDA inspectors have or have not visited every plant that exports into API or finished drug products in the United States?

Andrew von Eschenbach: I'm going to take that in two parts. First I'm going to ask Mike Rogers to speak specifically to the issue of inspections and how we approach that from a risk based point of view and the process that's involved.

Then I'm going to take it immediately following it to answer your somewhat larger question as to how are we attempting to address the issue of an increasing number of products that are produced outside of the United States and require oversight that must occur beyond our borders.

Mike?

Michael Rogers: Thank you Dr. von Eschenbach. It's important to note that FDA's foreign inspection program is primarily driven by the product approval process, that effort to make medically necessary products available to American consumers.

Firms that are referenced in applications are targeted and identified using a risk-based approach. And the approval of an application is triggered by inspections of a firm's reference in these applications.

We recognize that the science board report did identify some challenges and gaps with respect to our inspectional history over time.

But overall, the approval of an application is typically triggered by an inspection of the companies referred to in that application.

Julie Zawisza: David, could you hear that?

David Greising: I heard it but I'm not sure it was directly responsible - responsive to the question which is, and maybe you can clear this up for us, you're saying it's a risk-based system.

I think people want to know you know does an FDA inspector in fact visit these plants minimally, does it do that - does somebody from FDA visit these plants prior to inspection - prior to shipping to the United States, or perhaps they don't.

Perhaps they just review paperwork, and if so is at least paperwork reviewed for these plants prior to shipment to the United States or do some just begin shipping without any oversight at all?

Janet Woodcock: This is Janet Woodcock. Our policy is before - with a new plant before it's marked - importing an ingredient into the United States, we will have a pre-approval inspection, all right?

If we've been in any plant around - within the last several months say, or we have observed that plant, we may review paperwork, all right.

But our policy is for any plant that we do a pre-approval inspection. We don't get materials from plants that have not inspected.

Andrew von Eschenbach: What is important we're trying to address here is the fact that inspections vary depending on what it is we're addressing.

And what Mike was trying to point out to you is that as it relates to those new products, products that are being requested for approval, we inspect those plants prior to that approval being granted.

Dr. Woodcock indicated that if we have information that we've inspected that plant very recently, we may work on that information. But that plant has to be inspected before - we have to have evidence of that inspection before we approve that product.

That's different then from going to plants because we are going back to do routine surveillance. And across the board we're taking a risk-based approach.

Some plants that are producing medical products like a device like tongue depressor do not create the kind of risk that would require us to be looking at them on a very, very frequent basis.

And there may be very, very long intervals between those inspections, whereas others where the product is of much greater concern, then that inspection frequency would be increased.

Overall, we recognize that the number of sites that we must now pay attention to that are beyond or outside our border are going to require us to address that systematically.

Increase the number of inspectors available to carry out those inspections, move FDA presence beyond our border so that we have opportunities to be closer to where those plants are, to be able to be more engaged.

Three, build capacity with our foreign counterparts and other countries who are also engaged in inspections and be able to amplify our ability to address what is an increasingly global market and global production.

David Greising: And thank you Dr. von Eschenbach, but if I might just follow up with one question.

Julie Zawisza: Quickly please.

David Greising: This is the last one. The science board report said and know I'll quote it, "Millions of FDA regulated products are imported into the country each year from foreign facilities that have never been inspected by FDA and with current appropriations never will be".

Do you agree with that statement, or do you disagree and can you tell us why in either case?

Andrew von Eschenbach: As I've just tried to explain to you, if you go out to the product that we're talking about, a blanket statement like that really needs to be put in the context of what specific product are you addressing.

And as I tried to indicate and I don't want to be glib about this, the issue of a need to inspect a plant that's making something that is of such low risk as a tongue depressor even though it's an FDA regulated device, is much different than inspecting a plant that's making an active pharmaceutical ingredient for a critical drug.

And I think the blanket statements are not applicable. We really need to look at this in the context of what is the product, what is the source, what is the degree of risk, and what is the most effective way to utilize the resources that we have.

An FDA inspector uses information and reports that are available to us, confidentiality agreements that tell us about that site by virtue of the fact that someone else has recently inspected it and relationships with the local agencies in those countries who are also providing oversight.

So again, I hope you'll put this into a context that really addresses the complexity of the problem and I'm not by any stretch of the imagination not indicating that we do not have to do more in order to continue to be responsive to the increasing, demanding complexity.

And - but at the same time, it's a matter of doing the right thing and doing it in the right way. And I hope you'll understand that a simple answer to a complex question is not going to serve helping to - help people understand how and what we are trying to do.

Julie Zawisza: Thank you Dr. von Eschenbach. And I'd like to keep this moving folks so let's take the next question.

Coordinator: And next is Lauran Neergaard with the Associated Press.

Julie Zawisza: Go ahead Lauran.

Lauran Neergaard: Hi, thanks, I have a question for Dr. Woodcock and then another follow up for Dr. von Eschenbach.

Dr. Woodcock, the 5 to 20% that you referenced, are those coming from the Changzhou plant or because there are multiple - there are at least two consolidators supplying to SPL.

Are we now talking about different plants that have to be inspected?

Janet Woodcock: We're pursuing our investigation, okay? What we're saying is of the samples we have tested which are primarily APIs, that's the range we're seeing that we've - it's been a limited number since we just discovered these tests.

And we will have more information later. We're obviously pursuing all these aspects as we speak.

Lauran Neergaard: And Dr. von Eschenbach, to take your tongue depressor analogy a step further, can you tell us what proportion of plants in China are these low risk tongue depressor type? And what are higher risk types like those involved with heparin or other drug products?

Andrew von Eschenbach: You know I can't give you that answer specifically right off of the top of my head today. I think it's fair to say that we have to continue to make a very concerted effort at being able to define the plants that we have to be addressing and paying attention to.

And let me be specific about that as it relates to China. One of the things - a memorandum of agreement with China has addressed is that from the Chinese perspective as they register plants that are making products, there are some plants that are registered as simply being chemical manufacturing facilities, which would not fall under an FDA inspection - a blanket if you will.

And yet we recognize from our end that the product that's being developed is actually a chemical that's turning into an active pharmaceutical ingredient in which case we do need to inspect that.

So we're trying to reconcile and be able to enhance the completeness and accuracy of even the databases upon which we have to make these decisions.

So I can't give you the absolute numbers. Mike Rogers will indicate to you some scale and scope of the number of facilities that are subject to inspection, and the fact that this year we've done more foreign inspections than ever in the history of the FDA.

Mike, do you want to add to that?

Michael Rogers: Yes, thank you. I think that's right, let's emphasize that the agency this year reported more foreign inspections than we ever have in the history of the program.

We believe we do more than any other regulator in the world, we believe and others have associated us with the gold standard. So we recognize that this is a complex situation.

But we don't believe, as Dr. von Eschenbach mentioned, that inspections are the only part of this issue.

Efforts to collaborate with foreign governments, efforts to test products at the border, information that we can learn from our domestic inspections as well as our foreign inspection presence, and efforts to establish a presence overseas are all part of the big picture that we're working on now.

Julie Zawisza: Thank you and let's keep moving since we have a number of people on the line waiting to ask a question. Next question please.

Coordinator: Next it's Kim Dixon with Reuters, your line is open.

Kim Dixon: Hi, first question is can you give us an update on the number of adverse events and possible deaths that have been reported? And which - you know which do you think could be associated with the Baxter heparin?

Janet Woodcock: Yes, this is Janet Woodcock. We have a total of 785 reports, and as we said a week ago that we had 21 reports of death, okay.

We actually have received more reports of death, up to 46 total reports, okay. But many of those do not fit our definition of this type of event, because the deaths are just in someone who might have used heparin.

And many of them are at different times, not necessarily recent. Because whenever there's an announcement about a product problem, it triggers a lot of people to send in their reports.

Kim Dixon: Right.

Janet Woodcock: So right now, we have evaluated these 46 reports and of reports about heparin since January 1st, 2007, we see 19 total deaths.

Kim Dixon: Okay. And then 785 are those, how many of those do you think are related to the heparin and are those all serious adverse - severe adverse events?

Janet Woodcock: They are serious, but they are - we have not gone over all of them. As I said they are continuing to come in fairly rapidly because there's been a lot of press reporting of this.

And so people have been reporting and we have not gone over each one of these and seen it - whether or not it fits this anaphylaxis with - and hypotension definition which is what we're seeing in this particular cluster.

Julie Zawisza: Thank you, let's go to the next question please.

Coordinator: Next is Ricardo Alonso-Zaldivar with the LA Times.

Ricardo Alonso-Zaldivar: Thank you for the update and from Dr. Woodcock, getting back to the contaminant that you discovered in this product, what would have been the effect of that contaminant in conventional testing?

Is it something that would have made the product seem more potent? Could you explain a little bit about that?

And also as a follow up, did Baxter wait too long to alert the FDA that there was a possible problem here? Thank you.

Janet Woodcock: The first one is, the product - the contaminant has as I said earlier some activity in the identity test for heparin. So that's a reason that an API that had this contaminant in it would perhaps not register having anything abnormal as far as its identity as heparin, all right?

And so I think that answers your first question.

Ricardo Alonso-Zaldivar: So in other words would it have seemed in the conventional testing, I mean is it something that could have been added to make it seem you know like it was pure heparin or…

Janet Woodcock: Well it - say if you had 20% of something else in heparin instead of heparin, then the heparin would have tested as sub-potent, right, as not enough there in the identity test.

But if you - or in the potency test, the bioassay that's done, if you had this substance, it appears from what we know so far, that it appears - it acts like heparin in this test, and so it looks like everything's fine when you do the test.

Julie Zawisza: And what was your second question Ricardo? Let's move on to the next caller then.

Coordinator: And our next question comes from Marc Kaufman with the Washington Post.

Marc Kaufman: Yes hi, two questions, the first getting back to the adverse events and the deaths, I was somewhat confused by the numbers, Dr. Woodcock, you had made reference to January 1st 2007.

Janet Woodcock: Please speak up.

Julie Zawisza: Yes.

Marc Kaufman: I'm sorry, in terms of the adverse events, you made reference to January 1st 2007, and that there were 19 total deaths that appeared to be related to heparin. Did you mean January 1 2008?

Janet Woodcock: No, we received the reports in the last three months, but the events occurred over the last 14 months. That's what's very confusing.

Mark Kaufman: I see.

Janet Woodcock: You might have received a report this week, but it refers to events that occurred last August.

Mark Kaufman: Gotcha, okay. And the 19 total deaths are ones that after doing a review you have concluded meet the criteria of the kind of problem that you're seeing, associated with an adverse event.

Janet Woodcock: That's correct, they look like the kind of event that we're looking at. We see many you know reports of different things that happen to people.

Here we're talking about anaphylaxis or hypotensive events.

Marc Kaufman: Okay. And getting back to the contaminant, I have to admit I'm confused here. Is there any guidance you can give us in terms of whether or not this appears to be something that was added intentionally or is this something that could in the normal processing be a mistake that somehow comes about?

And as a corollary, has it ever been seen before?

Janet Woodcock: We have no information it's been seen before, right? As we said earlier we do not know whether this was - occurred by some error or some biological process or something or happened deliberately.

We do not have that information at this time, we are actively investigating both of these possibilities.

Julie Zawisza: Thank you, let's go to the next question. Do we have another question, another caller? We've got just a few more minutes here if anybody has a question that hasn't been answered.

Andrew von Eschenbach: Let me just add on to the previous question, I think what Dr. Woodcock was mentioning is that the sophisticated chemical analysis of this contaminant is ongoing.

And then further understand the process by which heparin is made so that it can be better determined whether its presence is something that is an error in manufacturing or whether it was an intentional contaminant or contamination, adulteration.

At the same time the important other point to be made is that having begun to identify this contaminant, we've been able to create test kits that are - or have access to test kits that can pick it up and determine it now that we have a better idea of the kind of thing we're looking for.

And those test kits we expect to be able to be made available so that current sources or current distributions of heparin and its active pharmaceutical ingredient can be checked to be certain and to verify that this contaminant is not present.

So it is important to point out that in addition to just doing the analytical processes in these sophisticated laboratories, we're also developing some tools to be able to be more widely dispersed to be able to check other heparin quantities or sources to be sure that they're free of this contaminant.

Janet Woodcock: Yes, this is Janet Woodcock. What we'll do is within the next several days we'll be posting analytical methods, and we are exploring developing some reference material as well for people to use.

Julie Zawisza: Thank you that was Dr. von Eschenbach then Dr. Woodcock. Let's go to the next question please.

Coordinator: Next comes from Anna Mathews with Wall Street Journal.

Julie Zawisza: Hi Anna.

Anna Mathews: Hey. Thanks, I (unintelligible) not to be asking this but I'm really confused. So again back to the deaths, I just need to clarify, I thought that Dr. Woodcock said initially the 19 total deaths that you had reports of that occurred since the 1st of January 2007.

I thought she had said that FDA had not gone over all of them and is not sure if they've - that the description of anaphylaxis and hypotension, but then in an answer to a question she said no, yes all 19 of them do look like that kind of event .

Janet Woodcock: Yeah, you are confused. When I said this - what we haven't gone over and we're talking about this 785 reports.

Anna Mathews: Okay. So the 19 deaths all fit the description of concern. And all they are - did they all occur in users of the Baxter product?

Janet Woodcock: Well a lot of times the people do not file what product, you know they don't submit to us what product was used. So we can't assess that in some of the situations.

Anna Mathews: Do you know how many of the 19…

Julie Zawisza: (Unintelligible) the next question?

Coordinator: Okay, and next is Lisa Stark with ABC News.

Julie Zawisza: Hi Lisa.

Lisa Stark: Hi, can you hear me?

Julie Zawisza: Yes.

Lisa Stark: Okay, sorry, I wasn't sure if my mute button was on. I just want to clarify one thing that I'm a little confused about. Do you know for certain that this contaminant was introduced either - I know you don't know whether it was deliberate or not, but do you know for certain it was introduced in the Chinese plant, or is there still - is that still not determined for sure.

Could it still have been in the Wisconsin facility or is it definitely introduced in the Chinese facility?

Janet Woodcock: Good question. We do not know where it was introduced or how - as we said how it got into this - these products, these API products. We do not know that at this time.

Lisa Stark: All right, thank you for clarifying. Then my one question is, during the whole pet food issue of course as you know there was sort of this filler put in that seemed to be able to allow the pet food to pass all the tests.

And - but was less expensive and not the proper ingredient for the pet food.

Janet Woodcock: Right, I kind of remember that.

Lisa Stark: Yeah. Do you have a sense, could this be a similar thing where you're - it's substituting some less expensive ingredient that will pass all the tests but isn't kosher when it comes to the drug you're trying to make?

Janet Woodcock: It is possible. We - as I said we still don't know whether this was - inadvertently got into the supply or whether it was actually added.

Julie Zawisza: Thank you.

Lisa Stark: Thank you.

Julie Zawisza: Next question please?

Coordinator: And the next question comes from Miriam Falco with CNN Medical News.

Julie Zawisza: Go ahead Miriam.

Miriam Falco: Hi there, thanks for taking these questions. I was a little confused about the Wisconsin and China thing too, I'm glad that was clarified. You do not know what this contaminant could do, correct, in a negative way. You just know that it mimics what heparin is supposed to do, is that correct?

Janet Woodcock: That's correct.

Miriam Falco: Okay, and in terms of the inspection, in last week's telebriefing you mentioned that when I asked about have you inspected the facility when you should have, you said that the inspection would have occurred in 2004.

This cropped up in 2007, so you wouldn't have caught it. And you also explained that you only - your primary goal for inspection is in the approval process.

So something has been approved for many years, you don't return? I mean how often do you revisit a place? Things change in companies.

Deborah Autor: Yeah, this is Deborah Autor. I think you spoke to me last week about that, and what I said is that there's no reason to think that we would have picked up the issue in 2004 given that the SPL facility shipped heparin API problem free for years as far as we can tell.

In response to the question of how frequently we go back to each facility, as Dr. von Eschenbach explained, it depends on the nature of the product, it depends on our resources, it depends on our other priorities.

We use a risk-based approach which drives when we are able to go back to any given facility given our resources.

Miriam Falco: But then in this particular case, we're talking about heparin now, not about the tongue depressors. If there wouldn't have been a - basically a problem has to occur because - before you would revisit it?

Deborah Autor: No, not necessarily.

Andrew von Eschenbach: This is Andy von Eschenbach again. It's really important to emphasize the fact that we're looking at this across the entire spectrum of prevention intervention kind of response.

There are circumstances in which a product may have been around, let's say that heparin has been around for sixty years, in which there hasn't been a history of any problems whatsoever.

And then either intentionally or unintentionally someone manipulates that product. We may not be at that plant at that particular point in time under any - under even the best of circumstances.

And that's why we have to have in place a very strong response system, so that we detect the signal of an adverse event as we did in this situation, we immediately can respond in a methodical and effective way to mitigate that outcome.

At the same time we also have to have in place processes that will enable us to intervene, and whether they are inspections at the border or other ways of surveying and overseeing, working with our partners and collaborators, we need to keep track of what's going on.

And then we also have to have inspections. But it's - would be disingenuous for me or FDA to be suggesting that under every circumstance in every case,

we would be able to be inspecting every single production facility around the entire world that's making every single kind of medical product.

So we have to approach it in a much more strategic kind of way. And what I think Dr. Autor is explaining is that in 2004 when we were investigated- would have inspected this plant, this problem was not occurring. It wasn't apparent.

And the problem probably didn't even exist at that point in time, so any inspection whatever would have not picked up the issue. That's why we have to have all these parts in place.

And I hope that that's not lost in the importance of this story in terms of what FDA - how FDA is trying to approach this strategically and systematically across the entire life cycle of the products we are responsible for regulating from the very beginning of their production all the way through to their delivery to patients or to the public.

Julie Zawisza: Thank Dr. von Eschenbach. Folks we have a number of people who still have questions, we can't take them all but this is a very important discussion we're having so we'll take as many as we can and let's take the next one.

Coordinator: Next is Jennifer Corbett with Dow Jones, your line is open.

Jennifer Corbett: Yeah, I have a question about where exactly in the supply chain you found the contaminants. I mean are you - were you looking at finished product, the actual recalled product?

It sounds like this is much earlier in the process.

Janet Woodcock: We have found it in the API and in the finished product. We're pursuing further investigations now, yeah upstream and so forth but we do not have those results yet.

Jennifer Corbett: Okay, thank you.

Julie Zawisza: Thank you, next question.

Coordinator: And the next question comes from Karl Stark with the Philadelphia Inquirer.

Julie Zawisza: Hi Karl.

Coordinator: And Karl just…

Julie Zawisza: Dropped off.

Coordinator: Yes.

Julie Zawisza: Okay, if he comes back in let us know, let's take the next one.

Coordinator: It will be one moment please. And the next question comes from Peggy Peck with MedPage Today.

Julie Zawisza: Hurry up please.

Peggy Peck: Yes, this is Peggy Peck, thank you very much. I'm really interested in this test, if I understand that identified the contaminant. If I'm understanding this correctly, Dr. Woodcock you said that you - the phrase that I wrote down was "We just discovered this test".

And I'm wondering if you can just tell me a little bit about the process of discovering the test that discovered the contaminant.

Janet Woodcock: Yes, I guess what I said was we just discovered the contaminant. We just - what you usually do when you're investigating problems with a medicine, a drug, is that you run a bunch of chemical analyses on there.

You have some ideas of what you might be looking for depending on the reaction and so forth.

The problem here is as we said earlier these are complex biologically derived molecules and the conventional testing didn't reveal this whatsoever and it took a little while to find the correct test.

And even when we found a signal, took a little bit longer to verify what it was in there that was making that signal on some of the analytic tests.

So it was a, you know classic chemistry investigation where we figured out finally the proper test. We still haven't totally nailed down the actual chemical structure of this so we can tell you it's this glycan.

But I think for most of the public, that's a little bit over their - you know level of interest anyway.

Peggy Peck: Just on follow, and I'm writing for a professional audience so I'm just wondering, you mentioned I think Dr. von Eschenbach mentioned earlier that there's been huge cooperation.

Did you have cooperation from sources outside the FDA as two which assay you should use to identify the contaminant or did this come from inter - inside the agency?

Janet Woodcock: Well we did a lot with our internal folks that we've had tremendous collaboration with the academic sector and experts in this area.

Julie Zawisza: Thank you, let's take the next question.

Coordinator: Next is Jill Weschler with the Pharmaceutical Executive Magazine.

Jill Weschler: Hi, thanks for taking my question. I just wanted to clarify that you have found this contaminant in API from the Wisconsin facility, and is that because you haven't run these same tests on API from the Chinese facility?

And also that you have found this contaminant in the finished product from Baxter.

Julie Zawisza: We should go over again what samples we've collected and what we've found.

Janet Woodcock: Okay. The contaminant is present in heparin API that's produced by Scientific Protein Labs which has facilities in China and Wisconsin. And we found the contaminant in APIs that emanated from those.

And we can't say any further like where it started basically. So is that clear?

Jill Weschler: Yes, so it was in some of the APIs from the Chinese facility is that correct?

Janet Woodcock: Yes. It originated there, the API originated there. We can't tell you where the contamination originated. The API did originate there.

Jill Weschler: All right, thank you.

Julie Zawisza: You're welcome. And ladies and gentlemen, we have time for one more question, so let's take that now.

Coordinator: And the last question comes from Chris Hollis with FDA News.

Chris Hollis: Hi, thanks for taking my question. I wanted - you guys said a number of - record number of foreign inspections, do you have a number? An exact number?

Michael Rogers: Yes, this is Michael Rogers. That number, the headline you should take away from this is in FY07 as you heard the agency reported more foreign inspections than we ever have in our history.

That number was over 1000. It's also a record number for overall drugs inspections as well.

Chris Hollis: Okay. And I'm a little confused, API is made in both Wisconsin and China, the SPL facilities? Or is it just coming from China and then to the Wisconsin facility for shipment to Baxter?

Janet Woodcock: It is - it's made also in Wisconsin.

Chris Hollis: Okay.

Janet Woodcock: But the source is - there are other - the source material isn't necessarily from Wisconsin.

Chris Hollis: Okay. And just one more question, is the FDA going to be requiring manufacturers to use more sophisticated identity tests now considering this…

Janet Woodcock: You know this gets to our quality by design issues, and I won't bend your ear on this, but we - you know one of the things that we believe is that in general with pharmaceutical manufacturing needs to have better science and use the most advanced scientific technologies both to test and to manufacture their products.

And as you may know over the last four to five years we've had a huge initiative on that. We're really looking at this as new applications come in.

You know what type of understanding does the manufacturer have about both the APIs, the other materials, and their process so that they really have a grip on their products.

I'm not saying in this instance there was anything done wrong, I mean it met all the, you know, the current tests that were done on this product that were conventional tests.

However in the future we're really encouraging much more advanced science.

Julie Zawisza: Thank you Dr. Woodcock. Ladies and gentlemen, this concludes our briefing today and I'd like to thank you for your participation.

And we'd like to thank our speakers Dr. von Eschenbach, Dr. Woodcock, Mr. Rogers, Ms. Autor and Dr. Nasr.

If you have questions following this briefing and we suspect that you may, please call the press office, ask for Karen Riley or Brad Swezey, 301-827-6242.

And I want to remind you that as we said earlier that we will have ongoing briefings, periodic regular briefings as new information comes out that we can impart to you and we certainly appreciate you reporting on this.

And you have a very nice afternoon, thank you.

Coordinator: And that concludes today's call, please disconnect your line at this time.

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