**Transcript for FDA's Media Briefing on the FDA's Review of the ReGen Menaflex**

**HHS FDA**

**Moderator: George Strait**

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**4:58 pm CT**

Coordinator: Good afternoon and thank you for standing by. At this time all participants are in a listen only mode. After the presentation we will conduct a Question and Answer session. To ask a question at that time, please press star then 1. Today's conference is being recorded, if you have any objections, you may wish to disconnect at this time. I will now turn the meeting over to Mr. George Strait. Sir you may begin.

George Strait: Thank you (Susan). And thanks everyone who has called in. Today's meeting and briefing is to discuss a report on the FDA's review of the ReGen Menaflex, a medical device used in surgical procedures for the reinforcement and for repair of soft tissue injuries of the medial meniscus.

The report has been posted on the FDA Home Page. At the media briefing to answer questions is Dr. Joshua Sharfstein, who is the Principal Deputy Commissioner for the Food and Drug Administration; and Dr. Jeff Shuren, who is the acting Director of the Center on Devices and Radiological Health, CDRH.

I'll start with Dr. Sharfstein, and we'll have a few comments.

Josh Sharfstein: Good afternoon. This is Josh Sharfstein; I'm the Principal Deputy Commissioner at FDA. This report originated out of concerns that we were made aware of through Congress and through the media, about the review

process for this particular device and whether FDA's review process had integrity.

And on the basis of those concerns, when I was the Acting Commissioner, in May we - I asked the Acting Chief Counsel, Mike Landa; the Acting Chief Scientist, Jesse Goodman; and the Associate Commissioner for Policy and Planning, Dr. Jeff Shuren, to lead a review of this - a clearance process targeted at several questions, including, "Were established procedures and processes followed in the review of the device?"

In addition, I think I asked, "Was the integrity of the advisory panel process compromised?" "Was the integrity of the review process compromised?" "Should the decision to clear the device be re-evaluated and what changes to FDA's policies, processes, or procedures should be considered to protect the integrity of FDA's decision making?" And the - those three officials oversaw a review that I think you have. It's on the FDA Web site, it is quite detailed.

It finds that there were in fact numerous departures from processes, procedures and practices and that there was a definite threat - and problems with the integrity of the review process for this device. It makes a series of recommendations, all of which will be adopted. And those include review of the 510(k) process, which we announced yesterday would be conducted by the Institute of Medicine.

It also includes a re-evaluation of the clearance of this device, which will occur. It - and the recommendations include a place in the Commissioner's office for a contact and appropriate relationship with the companies that have concerns. And it includes a more clear set of procedures for resolving differences of opinions within the Center for Devices and that’s forthcoming relatively shortly.

I think that there are a lot of details in the report, but from my perspective, the message here is that there were problems -- with the integrity of FDA's decision making -- that have solutions. And FDA is committed to the integrity of its decisions and we will take the steps necessary to protect that, both from - you know, from concerns of various types that can affect the decision making.

And I think that's basically all I'd like to say by introduction. And we're open to questions.

George Strait: We'll now entertain your questions. Please identify your media outlet and, we have time for one question and one quick follow-up.

Coordinator: Thank you. We will now begin the Question and Answer session. If you would like to ask a question, please press star then 1. Please un-mute your phone and record your name clearly when prompted. To withdraw your request, press star then 2.

Once again, if you do have a question, please press star then 1. One moment please.

Our first question comes from Lindsey Layton, Washington Post. You may ask your question.

Lindsey Layton: Thanks very much. Good afternoon. I think that for consumers the primary question in their minds may be whether this product is actually unsafe. And when you say that you're going to be reviewing the approval process, what happens in the mean time? Do you pull it from the market? Does the

manufacturer? Or do you request them to stop using it? What is the status of this product and is it safe? Thank you.

Jeff Shuren: This device has been cleared by the FDA. And we have no basis to question the safety of this device. So it will remain on the market. What we have concluded is the integrity of our process for reaching a decision was compromised in this case and so we are revisiting and re-evaluating the record and the basis for making that decision.

Josh Sharfstein: And let me just add from my perspective -- that was Dr. Shuren, this is Josh Sharfstein -- that there are a number of situations that we face at FDA where different types of questions come up about products. While we investigate those questions, they generally are on the market.

And we're transparent about what the concerns are, just like we are in this case; posting our - the issues that relate to the process for decision making so that people can understand that the issue - it's similar in some ways to when CDER says that we're investigating a concern about the safety of a drug, that if a - the drug doesn't come off the market in the interim. So I think that this is an appropriate from - way of handling it, both from a policy and a legal standpoint.

Lindsey Layton: Can I ask a follow-up question?

George Strait: Sure.

Lindsey Layton: There are a number of other devices that were - that questions have been raised about regarding the appropriateness of the review process, and I'm wondering are you now going to go down a list and look at other products?

Josh Sharfstein: This is Josh Sharfstein again. This is a pretty unique situation that led to this report. There were really extraordinary concerns raised about the integrity of the review process. It wasn't so much people had a question about the device or a particular issue. This was really about the integrity of the whole review process. And we really feel like we've - the reason to look into this one at this kind of detail was to understand what changes needed to be made for the whole program.

And Dr. Shuren -- who was the Associate Commissioner for Policy and Planning and is now the Acting Center Director for Devices -- is moving very quickly in a number of areas to strengthen the device program. And I think that our approach is going to be to support him in the things that he's doing for the center as a whole.

But in terms of other reports like this one, I don't think it's likely you'll see a lot of these. This we really think was an extraordinary circumstance.

George Strait: Next question please.

Coordinator: Susan Heavey, Reuters, you may ask a question.

Susan Heavey: Hi, thanks for taking my call. This follows the announcement you guys had yesterday that the IOM was going to conduct this study [of 510(k)'s], and seems to be part of this larger issue with the device center. I was wondering if you could touch on; One, some critics saying that 2011 [when the report is completed] is really going to take - it's too long to find out what needs to be done at the agency.

Jeff Shuren: Yes, well one of the other things that we are doing is we are doing our own internal review of the 510(k) process to look at opportunities to tighten up the

program under our existing authority. And if there are issues that are raised regarding that program, wherein we would need the help of Congress, we will go back to Congress and raise those issues with them.

Josh Sharfstein: And this is Josh Sharfstein. I think that the reason we think that that very in-depth look by the Institute of Medicine is important -- and why I think people who have looked at this have agreed with that -- is that it has been quite a number of years, several decades, since this program's been set up and it really deserves a thorough look to see whether its processes are aligned with public health.

And that includes both safety and innovation, which is a very important part of public health. But, you know, we want to see [that] effective and innovative device[s] [are] getting to market as quickly as possible. And that the kind of thoroughness that the Institute of Medicine can bring to it will be helpful.

That doesn't mean we can just freeze the process in place in the mean time. And you heard from Dr. Shuren that in fact, there's going to be a group looking at interim changes that can be made. And if there are things that come up, we will do those. But I think we're really thinking big when it comes to devices; that we really want to see the full set of recommendations taking stock of the process on both the safety and the innovation side.

Susan Heavey: Thanks.

George Strait: Got a quick follow-up?

Susan Heavey: No I'm all set, thanks.

George Strait: Next question please.

Coordinator: Alicia Mundy, Wall Street Journal, you may ask your question.

Alicia Mundy: Hi everybody. I have a couple of just fast questions here. The first is just; did you interview Dr. Von Eschenbach for this report?

Josh Sharfstein: I think there's a footnote that discusses that he declined to be interviewed...

((Crosstalk))

Alicia Mundy: Okay, sorry, I hadn't gotten to that. Then my main question is on Page 1, you were talking about the 17-year review. And you talk about - you talk fairly eloquently at some point about predicate creep. You say at the very end of what is marked as Page 1, "that because the 510(k) review process relies on predicate devices, the failure to sufficiently explain how the predicates worked in this will almost certainly effect subsequent review decisions."

In a way, that seems to be signaling me that this device - that the review of this device may not be positive in that -- if I'm interpreting that sentence correctly -- you're already questioning the basis of it as a 510(k). Can you explain a little bit more?

Josh Sharfstein: Now, that's not how I would read this...

Alicia Mundy: Okay...

((Crosstalk))

Josh Sharfstein: I understand the question, but it's not how I would read this. I think the idea here is that one of the major findings of this was that there was not adequate

explanation in the record. And when there's not an adequate explanation, it's hard to apply the predicate standard, because it relies on really understanding the clearance.

So that's not - it really doesn't speak at all to the safety of the device, it speaks to the adequacy of the explanation. And I - it could certainly be that when the re-evaluation happens that we find the device is perfectly, you know, meets all the criteria and it could wind up to be the same decision. But...

Alicia Mundy: Okay.

Josh Sharfstein: ...what this is saying is, if we do do that, and we go through that process, there will then be the explanation in the record that will allow that to be used as a predicate device according to the law.

George Strait: A quick follow-up, Alicia?

Alicia Mundy: Yeah, the next sentence says it's - you've already received a - I guess applications citing the Menaflex as a predicate. Are you allowed to describe what kind of devices are now citing Menaflex as one of their predicates?

Josh Sharfstein: I don't think we're allowed to...

Alicia Mundy: Okay.

Josh Sharfstein: ...(unintelligible).

George Strait: Okay, thank you. Next question please.

Coordinator: Gardiner Harris, New York Times, please ask your question.

Gardiner Harris: Hi, I want to just go back to a follow-up of Lindsey's question, and that is; what is your message to patients who have gotten this device implanted in their knees? There's clear, in the record, previous FDA scientific reviewers who have called this device unsafe, and certainly said that this device was not proven to be safe and effective. I'm just wondering if you - what you say to those folks?

Josh Sharfstein: I think I would say that, "This report is not a reason to panic. This is a - the FDA is going back to make sure that the clearance of this device is handled well. Just like, if there were a question about another type of product, we would take extra steps to make sure that those products are appropriate."

But there - this is not a review that finds a specific safety problem with the device, this is about the process and that at this point, I would advise any patient to talk to their doctor. Their doctor can review this report and decide whether this would affect her or his decision, but that this is really about the approval process, and not the safety of the device itself. This is not - we're not issuing a warning to patients, and one is not justified at this time.

Gardiner Harris: Are you going to review - in other words, is the approval of this device not subject to further review?

Josh Sharfstein: No, no. The - I'm not sure what you mean by that, but I think...

Gardiner Harris: In other words, are you going to sort of reassess whether the device should be approved?

Josh Sharfstein: Yes, yes, we are.

Gardiner Harris: You are reassessing whether it should be on the market at all?

Josh Sharfstein: That's right. That was the recommendation of the group on the basis of the fact that there were such a significant problems with the process that led to the approval. In the end, this was approved by very senior people at the agency. And it is on the market.

And, you know, the concerns we have are about the process that led to the approval, not about specifically the safety of the device. So we are going to re-examine that question because we think that's the right thing to do. But patients should know it's not a specific safety issue that has come up that led us to do that.

George Strait: Thank you. Next question.

Coordinator: Matt Perrone, Associated Press, you may ask your question.

Matt Perrone: Hi guys, thanks for taking questions. It - this report talks a little bit about, you know, the really aggressive lobbying that went on here and sort of raises questions about, you know, staffers' ability to, you know, be protected from that. What type of recommendations did you make to make sure that that really doesn't play any part in, you know, the scientific process here?

Josh Sharfstein: I think that, taken broadly, this report is about how the scientific decision making process can be strengthened in general, from many different aspects.

And one of the points in here is that the company, for example, can be interacting with a particular office in the Commissioner's office as one of the

recommendations that would sort of be the lead, and would figure out the right time for an appeal, rather than, "I think there was a lack of clarity about that," was identified in the report and that led to some of the concerns that were found.

So I think that, there are multiple - I'm a - you know, every correction or recommendation that's in this report speaks to that because the stronger our underlying process is, the less likely it will be interfered with. So even if you take the questions that were raised about how clear the 510(k) approval process is, that lack of clarity that the report identifies is one of the things that made the process vulnerable. Fixing that is one of the ways to strengthen it, so it's harder for, you know, any external pressure really to influence.

I don't know - Dr. Shuren, you want to add anything?

Jeff Shuren: And on top of it, it's to make sure that when there are, you know, differences of opinion -- and that could be within the agency or with the agency and outside parties -- there is a very clear process to handle that, that is premised on fair hearing of different opinions, but also internal sunshine, so that the basis for someone disagreeing and a decision that's made by a manager is clearly documented in the record so that there's an adequate justification for taking that decision. And that was one of the failures that we saw in this particular case.

Matt Perrone: Okay, thank you.

George Strait: Next question please.

Coordinator: Jessica Bylander, The Gray Sheet, you may ask your question.

Jessica Bylander: Hi, thanks for taking my question. I'm wondering what legal authority FDA has to repeal a 510(k) clearance should the subsequent review determine that that's appropriate?

Jeff Shuren: In that circumstance we would move to reclassify the device. And we would up-classify it to a Class III, and then it would be subject to a pre-market approval application, rather than a 510(k).

Jessica Bylander: And, just a quick follow-up; has FDA ever done anything like this in the past?

Jeff Shuren: I'm not aware in a circumstance from a revisiting on a 510(k) decision to then up-classify. There are times with products on the market where we clearly have up-classified them with experience over time, where we're aware that there are new risks that are - that we're aware of that would cause us to change the classification. In fact we did that recently in the case of dental amalgams, and we up-classified that from a Class I to a Class II.

Jessica Bylander: Okay.

Josh Sharfstein: And I think this may relate, I'll look at Jeff, to sort of conjunctionally to the issue that the GAO identified that certain products need to be brought into the more modern regulatory system for - and FDA's going back and re-evaluating those devices. So that the re-evaluation of devices happens from time to time under this exact set of circumstances. This is more unusual.

Jessica Bylander: Thank you.

George Strait: Next question please.

Coordinator: Jared Favole, Dow Jones, please ask your question.

Jared Favole: Hi, thank you all for taking my questions. I have two, and they are; I'm confused as to how do you exactly go about, I guess re-reviewing whether this device should have been approved? Like what sort of steps are you going to take, and then when - the follow-up will be; when can the public expect a conclusion to that review?

Jeff Shuren: We are working out the process now, but our intent is to try to make a decision within the next few months.

Jared Favole: Okay.

George Strait: Thank you.

Jared Favole: Well, I guess that doesn't necessarily answer my questions. I'm still confused as to how you go about reviewing it.

Jeff Shuren: Well, we will have experts in the center that will review the data to see, first off, should this device be subject to a 510(k)? And if the answer is yes, is the science sufficient to conclude that this device should be cleared -- under the 510(k) standard? So it's the kind of review we otherwise would do in the agency.

Jared Favole: Okay.

George Strait: Thanks Jared. Next question please.

Coordinator: Mark McCarty, Medical Device Daily, please ask your question.

Mark McCarty: Thanks for taking the question. You mentioned something in the report about predicate creep, and one of the questions is; how much can you do from a strictly regulatory point of view by tweaking the regulations? And how much of a change in the 510(k) program addressing predicate creep would require a statutory change?

Man: (Unintelligible).

Jeff Shuren: Well this is one of the issues that we're looking for further study by the Institute of Medicine, and certainly we will look at it as well. I mean first is to decide, what - if there are any changes that should be made, what the appropriate policy should be and then to address what is the proper way to implement it. And that might be, if we were to make a change, that may be through regulation, it may require a change in law, but at this time this would sort of - we don't want to sort of pre-judge where the evaluation will go.

George Strait: Do you have a follow up?

Mark McCarty: No, that'll do.

George Strait: Next Question please.

Coordinator: Jennifer Smith, FDA Week, you may ask your question.

Jennifer Smith: Hi, I just wanted to double check, when you mentioned, Jeff Shuren, just about, I guess within - you mentioned something about there was going to be (unintelligible) clear procedures to resolve differences in opinion and (unintelligible) I think that was going to be starting soon. And that was also one of the six priorities identified yesterday in the statement by FDA, on the

announcement with IOM. So, I just wanted to a little hear more about that - what about these clear procedures to resolve differences of opinion?

Jeff Shuren: This will be - we will start with procedures for our own staff in the center, for what if there is a difference of opinion that may regard a matter of science or a matter of regulatory policy, and it can't be worked out informally. You know, the majority of times this has worked out amongst a review team.

But in some cases, there's a difference that can't be worked out that way. Here's the process by which that difference of opinion would be raised up through the management ranks, that there would be an airing of the differences, there would be documentation of the different positions, and then whatever decision is made, would also be clearly vetted and documented.

Josh Sharfstein: And then just let me jump into that...

Jennifer Smith: Sure.

Josh Sharfstein: ...for a second, this is Josh Sharfstein. It is not going to be possible to eliminate all differences of opinion.

Jennifer Smith: Sure.

Josh Sharfstein: And, you know, that's something that is, you know, part of the scientific process. And the purpose in, you know, looking at this is about the integrity of the process. And so we think that there will - it's likely that there'll be decisions that people internal to FDA may disagree with. But we hope to develop a process with greater integrity than we saw in this case so that we - people can understand what the decisions were, and how they were made internally, and that we can also have the process resistant to external pressure.

Jennifer Smith: Okay, and I do have a follow-up, but it's almost like a one - it's like a two part follow up. So let me just say it - it's essentially, so right now are there no formal procedures when there is like a difference of opinion, between like reviewer and manager? And then as part of that; B, are you looking at like the Equal Voice? What - which is what the Drug Center has instituted in the sense of having, you know, formal documents or what-not when it comes to difference of opinion.

Jeff Shuren: There are procedures in place; they are not nearly as rigorous as we believe that they need to be. And so we're changing those to provide that degree of rigor and transparency. But what's critical here is that there is an opportunity, when someone disagrees, that they get to voice (their disagreement) and that if a decision is made contrary to it, it's got to be well documented and well founded.

And we think that's critical in order to protect from a decision being made based on external pressure, where someone can make that decision, it's not clearly in the record why. If someone is forced to have to put that down on paper and justify it, it is going to be far more difficult (for) you to make a decision that's not well grounded in science.

Jennifer Smith: Well what's the Equal Voice?

((Crosstalk))

George Strait: Hold on, hold on, hold on, hold on.

Jennifer Smith: I'm sorry, I just want to like - that's part of that two-part question.

George Strait: I'm sorry, we give - we give - we give one question to one caller, you need to be fair to all of your colleagues so...

((Crosstalk))

Jennifer Smith: It's part of the same question.

George Strait: The next question please.

Coordinator: Virgil Dickson, FDAnews. You may ask your question.

Virgil Dickson: Thank you for taking my question. Josh, you had mentioned pretty early on in the conversation that in the end this was approved by pretty high up people. And this report you sent out today is addressing the process, but what about the individuals involved, is there something in place to address that concern as well?

Josh Sharfstein: Well I think this report is really about the process and how the process can (be) strengthened. This report is not about particular individuals. And I think if you, you know, have it - when you have a chance to read the report, you'll see that there are multiple weaknesses in the processes that were identified that we're committed to fixing.

Virgil Dickson: I guess, I understood that, I guess just to clarify, are there concerns about the people involved? Is - it's kind - because you'd mentioned that in the end this was approved by people - yes the process might have problems, but in the end it was still approved by people - so is that being addressed? Or do you have concerns about the people involved I guess?

Josh Sharfstein: No I think the context I was saying that is, you know, on what basis is it on the market, and you know, how can we - you know, where we're clearly leaving it on the market while this re-evaluation happens. And that is in part because it was in fact cleared by the Agency.

But as far as this report, it is really about the basic processes that underlie integrity at the Agency and not about individual people.

George Strait: Thank you all very much for participating in this meeting conference and briefing on the preliminary report of the agency's review of the ReGen Menaflex device. We will - we will - we will have this transcript available forthwith, and remember that the report itself is posted on the FDA Home Page and we thank you very much.

Coordinator: This concludes today's conference. Thank you for joining us. You may disconnect at this time.

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