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DEPARTMENT OF HEALTH AND HUMAN SERVICES

FOOD AND DRUG ADMINISTRATION

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CENTER FOR DEVICES AND RADIOLOGICAL HEALTH

MEDICAL DEVICES ADVISORY COMMITTEE

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GASTROENTEROLOGY AND UROLOGY DEVICES PANEL

+ + +

February 26, 2016
8:00 a.m.

Hilton Washington DC North
620 Perry Parkway
Gaithersburg, Maryland

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M E E T I N G

(8:11 a.m.)

DR. TALAMINI: I would like to call the second session of the February 25th and 26th, 2016 meeting of the Gastroenterology and Urology Devices Panel to order. It is now 8:11 in the morning.

I am Dr. Mark Talamini, the Chair of the Panel. I'm chairman of the Department of Surgery at SUNY Stony Brook on Long Island, New York, and I am a gastrointestinal surgeon by training and practice.

I note for the record that the members present constitute a quorum as required by 21 C.F.R. Part 14. I would also like to add that the Panel participating in the meeting has received training in FDA device law and regulations.

For today's agenda, the Committee will discuss and make recommendations regarding the reclassification for Urogynecologic Surgical Mesh Instrumentation, and classification for Hemorrhoids, Thermal, Device assigned to product code LKX; Hemorrhoids, Cushion assigned to product code LRL; Therapeutic, Automated, Blood Cell and Plasma, Separator Devices assigned to product code LKN. These devices are considered preamendments devices since they were in commercial distribution prior to May 28th, 1976, when the Medical Devices Amendments became effective.

Before we begin, I would like to ask our distinguished Panel members and FDA staff seated at this table to introduce themselves. Please state your name, your area of expertise, your position, and your affiliation.

And, Dr. Fennal, if I could begin with you. And we'll go around the room

counterclockwise, please.

DR. FENNAL: Good morning. I'm Dr. Mildred Fennal. I am a retired nursing professor from Florida A&M University. I currently act as the Director of the International Nursing Education Consortium. My background is critical care and advanced med/surg.

DR. DONATUCCI: Good morning. Craig Donatucci. I am a urologist. I am senior medical fellow at Eli Lilly, and I serve as the Industry Representative.

DR. IGLESIA: Good morning. I'm Cheryl Iglesia. I am a urogynecologist. I'm Professor of OB/GYN and Urology at Georgetown University School of Medicine, and I serve as the Division Director for the section of Female Pelvic Medicine and Reconstructive Surgery for MedStar Health.

DR. CARSON: Hi, I'm Sandy Carson. I am a reproductive endocrinologist and obstetrician/gynecologist. I am an adjunct professor at Brown University Medical School and the Vice President of Education for the American College of Obstetricians and Gynecologists.

DR. AFIFI: My name is Abdelmonem Afifi. I am a biostatistician, and I am a professor emeritus at the Fielding School of Public Health at UCLA, and I was the dean of that school for 15 years.

DR. TALAMINI: And, again, I'm Mark Talamini, Panel Chair.

DR. HICKS: I'm Terry Hicks, Clinical Professor of Surgery at LSU School of Medicine and Vice Chair of the Department of Colorectal Surgery at Ochsner.

DR. EFRON: Jonathan Efron. I'm Vice Chair of the Department of Surgery at Johns Hopkins and a Professor of Surgery and Urology and a colorectal surgeon.

DR. MARTENS: I'm Mark Martens. I am a professor of OB/GYN, and I'm Chairman at the Jersey Shore University Medical Center and Vice Chair at Rutgers Robert Wood Johnson School of Medicine, and I'm an OB/GYN.

DR. FISHER: Good morning, everyone. Ben Fisher. My background is in development genetics. I'm currently the Director of the Division of Reproductive, Gastro-Renal, and Urological Devices within the Office of Device Evaluation, FDA.

DR. TALAMINI: Thank you.

(Off microphone comment.)

DR. TALAMINI: Oh, on the phone we have Dr. Faulx. Would you like to introduce yourself, please, Dr. Faulx?

DR. FAULX: Thank you. I'm Ashley Faulx. I am an Associate Professor of Medicine at Case Western Reserve University and at Louis Stokes VA in Cleveland, and I am a therapeutic endoscopist and specialize in GI cancers.

DR. TALAMINI: Thank you.

And Dr. Louis DePalma will be joining us, and we'll have him introduce himself when he does.

If you have not already done so, please sign the attendance sheets that are on the tables by the door.

Lieutenant Commander Patricio Garcia, the Designated Federal Officer for this meeting, will now make some introductory remarks.

Lieutenant Commander Garcia.

LCDR GARCIA: Thank you, Dr. Talamini. And good morning, everyone.

I will now read the Conflict of Interest of Statement.

The Food and Drug Administration is convening today's meeting of the Gastroenterology and Urology Devices Panel of the Medical Devices Advisory Committee under the authority of the Federal Advisory Committee Act (FACA) of 1972. With the exception of the Industry Representative, all members and consultants of the Panel are special Government employees or regular Federal employees from other agencies and are subject to Federal conflict of interest laws and regulations.

The following information on the status of this Panel's compliance with Federal ethics and conflict of interest laws covered by, but not limited to, those found at 18 United States Code Subparagraph 208 are being provided to participants in today's meeting and to the public.

FDA has determined that members and consultants of this Panel are in compliance with Federal ethics and conflict of interest laws. Under 18 United States Code Subparagraph 208, Congress has authorized FDA to grant waivers to special Government employees and regular Federal employees who have financial conflicts when it is determined that the Agency's need for a particular individual's services outweighs his or her potential financial conflict of interest.

Related to the discussion of today's meeting, members and consultants of this Panel who are special Government employees or regular Federal employees have been screened for potential financial conflicts of interest of their own as well as those imputed to them, including those of their spouses or minor children and, for the purpose of 18 United States Code Subparagraph 208, their employers. These interests may include

investments; consulting; expert witness testimony; contracts/grants/CRADAs; teaching/speaking/writing; patents and royalties; and primary employment.

For today's agenda, during Session I, the Panel will discuss and make recommendations regarding the reclassification of urogynecologic surgical mesh instrumentation from Class I to Class II (special controls). The urogynecologic surgical mesh instrumentation is intended to aid in the insertion, placement, fixation, or anchoring of surgical mesh for procedures, including transvaginal pelvic organ prolapse repair, sacrocolpopexy, and treatment of female stress urinary incontinence.

During Session II, III, and IV, the Panel will discuss and make recommendations on the safety and effectiveness and the regulatory classification for the following classes of devices:

- Device, Thermal Hemorrhoids – intended to apply controlled cooling and conductive heating to hemorrhoids
- Cushion, Hemorrhoids – intended to temporarily relieve pain and pressure caused by hemorrhoids
- Separator, Automated, Blood Cell and Plasma, Therapeutic – intended to separate blood components and perform therapeutic plasma exchange for the management of serious medical conditions in adults and children

These devices are considered preamendment devices since they were in commercial distribution prior to May 28th, 1976, when the Medical Device Amendments became effective.

Based on the agenda for today's meeting and all financial interests reported by the

Panel members and consultants, no conflict of interest waivers have been issued in accordance with 18 United States Code Subparagraph 208.

Dr. Craig Donatucci is serving as the Industry Representative, acting on behalf of all related industry, and is employed by Eli Lilly Corporation.

We would like to remind members and consultants that if the discussion involves any other products or firms not already on the agenda for which FDA participants have a personal or imputed financial interest, the participants need to exclude themselves from such involvement, and their exclusion will be noted for the record.

FDA encourages all other participants to advise the Panel of any financial relationships that they may have with any firm at issue.

A copy of this statement will be available at the registration table during this meeting and will be included as a part of the official transcript.

Before I turn the meeting back over to Dr. Talamini, I would like to make a few general announcements.

Transcripts of today's meeting will be available from Free State Court Reporting, Incorporated.

Information on purchasing videos of today's meeting can be found on the table outside the meeting room.

The press contact for today's meeting is Deborah Kotz.

I would like to remind everyone that members of the public and the press are not permitted in the Panel area, which is the area beyond the speaker's podium. I request that reporters please wait to speak to FDA officials until after the panel meeting has

concluded.

If you are presenting in the Open Public Hearing today and have not previously provided an electronic copy of your slide presentation to FDA, please register with Mr. Jim Clark at the registration desk.

In order to help the transcriber identify who is speaking, please be sure to identify yourself each and every time that you speak.

Finally, please silence your cell phones and other electronic devices at this time. Thank you very much.

Dr. Talamini.

DR. TALAMINI: Thank you, Lieutenant Commander Garcia.

Our first speaker this morning will be Marjorie Shulman, Director of the Premarket Notification (510(k)) Program at the FDA, who will be providing a reclassification overview to the Panel.

Ms. Shulman.

MS. SHULMAN: Good morning. These are not my slides. Are they all together in one group? I apologize.

(Pause.)

MS. SHULMAN: The suspense is just killing you all, isn't it? It's just building and building.

(Pause.)

MS. SHULMAN: All right. Okay, are you ready? I just wanted to give the big buildup for this important talk.

(Laughter.)

MS. SHULMAN: Good morning. My name is Marjorie Shulman, and I'm Director of the Premarket Notification Program, also known as the 510(k) staff, and I'm going to talk about classification and reclassification.

So the purpose of the panel meeting today. Part 1 is to discuss the available scientific evidence regarding urogynecologic surgical mesh instrumentation, which is currently regulated as a Class I (exempt) device. You will be asked to recommend whether or not they should remain in Class I or be reclassified to Class II or Class III.

For Part 2, for three preamendment unclassified devices, you'll be asked to provide the FDA input on the classification for each of the devices to either Class I, Class II, or Class III.

So what are the different classes of devices? So the classification is based on the controls necessary to mitigate the risks associated with the device type. So for a Class I device, they're subject to general controls, Class II is general and special controls, and Class III is premarket approval. A device should be placed in the class, the lowest class whose level of controls provide a reasonable assurance of safety and effectiveness.

So what are the general controls? General controls are prohibition against adulterated or misbranded devices, good manufacturing practices, registration of the manufacturing facility, listing of the device types that are made there, recordkeeping, etc.

Special controls include such things as performance standards, postmarket surveillance, patient registries, and development and dissemination of guidelines.

Class I is for devices that general controls are sufficient to provide reasonable

assurance of the safety and effectiveness. Most Class I devices do not require premarket notification prior to being marketed.

There's also another area of Class I devices. Class I devices could be devices that cannot be classified into Class III because they're not life-supporting or life-sustaining, they're not of substantial importance in preventing impairment of human health, and they do not present a potential unreasonable risk of illness or injury, and also for devices that can't be classified into Class II because insufficient information exists to establish the special controls to provide reasonable assurance of safety and effectiveness.

So here are some examples of Class I devices: general surgical instruments, manual breast pump, and enema kit.

Class II is for devices that can't be classified into Class I because the general controls are insufficient to provide a reasonable assurance of safety and effectiveness, and there is sufficient information to determine what special controls could provide such assurance. So Class II devices typically do require premarket notification or a 510(k) prior to being marketed. But some Class II devices are exempt from premarket notification.

So some examples of Class II devices: fetal heart monitor, colonoscope, gastrointestinal feeding tube, and a hemodialysis system. Those are some Class II devices.

So how are special controls used? So as an example, cages were reclassified from Class III to Class II, and FDA issued a special controls guidance document to mitigate those risks to health, and it included such requirements as biocompatibility testing, material characterization, mechanical testing, sterility, and labeling for such things as warnings, precautions, adverse effects, etc. These special controls, in combination with the general

controls, provide a reasonable assurance of the safety and effectiveness. So the companies must provide evidence in their 510(k) submission on how those special controls were addressed.

Class III is for devices that cannot be classified into Class II because insufficient information exists to determine that the general and special controls are sufficient to provide reasonable assurance of the safety and effectiveness, and the devices are life-sustaining or life-supporting, or of substantial importance in preventing impairment of human health, or present a potential unreasonable risk of illness or injury. Class III devices typically require premarket approval, also known as PMA, prior to being marketed.

Some examples of Class III devices: extracorporeal photophoresis system, obesity treatment system, and implanted urinary and fecal incontinence device.

So what is the purpose of the meeting? Two parts. Part 1 is to discuss the available scientific evidence regarding urogynecologic surgical mesh instrumentation, which is currently regulated as a Class I device, a Class I (exempt) device. You'll be asked to recommend whether it should remain in Class I or be reclassified to Class II or Class III.

So what are we going to do? The decision to start the process is based on new information about the device, either on FDA's own initiative or upon the petition of an interested person. I think my 5 minutes was up. Okay. And the Agency can consider its intended uses which have been reviewed by the Agency.

So we would publish a proposed order of our proposed classification and seek public comment. That was done May 1st, 2014. We will convene a panel meeting to

discuss the proposed classification right now, and we're going to consider the public comments and available information, including Panel recommendations, prior to issuing a final order.

So this chart is just for your information on how we decide what class it would go in. If general controls were sufficient, it can go into Class I. If no, then you determine are special controls needed? If no, then it could be Class III for life-supporting and life-sustaining. And there's also that "Other" category that if insufficient information exists, it can go back to Class I.

What we ask from the Panel today is to review and discuss available scientific evidence regarding the safety and effectiveness of the urogynecologic surgical mesh instrumentation. And what that's going to include is to identify any risks to health presented by the device; whether the device is life-supporting, life-sustaining, of substantial importance in preventing impairment of human health, or presents a potential unreasonable risk of illness or injury; whether sufficient information exists to develop special controls; identify those special controls; and whether general controls are sufficient by themselves.

After the panel meeting we'll consider the available evidence, including the input of this Panel and the public comments. We'll issue a final order identifying the appropriate class. If Class I, the devices continue to be marketed. If Class II or III, the existing devices will remain on the market but either must submit a 510(k), a premarket notification, or a PMA in a specified time to continue to be marketed. If a 510(k) is not cleared or a PMA is not approved after that time, the devices will be considered

misbranded and must be removed from the market and distribution.

The second purpose of this panel meeting, Part 2, is for the three preamendment unclassified devices. You'll be asked to provide input to the FDA on the classification for each one, either Class I, II, or III.

A preamendment device was one that was introduced into interstate commerce prior to May 28th, 1976, which was the enactment of the Medical Device Amendments; however, it was not originally classified during that time where they classified the devices into I, II, or III. Therefore, no classification regulation exists for these devices. However, they do require a 510(k) at that time. So we're looking to classify it.

So the classification process for these preamendment unclassified devices is we'll receive a recommendation from a device classification Panel, publish the Panel's recommendation for comment along with the proposed rule classifying the device, and then publish a final rule classifying the device into either I, II, or III.

So for this part of the panel meeting, we're going to ask for your input on the classification of these devices into I, II, or III. The input is going to include an identification of the risks to health, if any; whether the device is life-supporting and life-sustaining, of substantial importance in preventing impairment of human health, or presents an unreasonable risk of illness or injury; whether sufficient information exists to develop special controls; the identification of those special controls; and whether general controls are sufficient for certain devices.

Again, this is the same chart again that you'd be following to place it into I, II, or III.

After this panel meeting, we're going to consider the available evidence, including

the input of this Panel and the public comments. We're going to issue a proposed rule proposing to classify the devices and seeking public comment. And after the final rule, if Class I or II, the devices can continue to be marketed. If Class III, we'll issue a separate call for PMAs, premarket approval applications. Existing devices may remain on the market until the submission of a PMA by a specific time frame, a specified time frame. And if the PMA is not approved, devices will be considered misbranded and removed from commercial distribution.

So that's that. It was worth the wait, right?

(Laughter.)

MS. SHULMAN: Thank you for your time.

DR. TALAMINI: Thank you very much, Ms. Shulman.

Any clarifying questions from Panel members on Ms. Shulman's presentation?

(No response.)

DR. TALAMINI: All right. Hearing none, we will now proceed with the Open Public Hearing portion of the meeting. Public attendees are given an opportunity to address the Panel, to present data, information, or views relative to the meeting agenda.

Lieutenant Commander Garcia will now read the Open Public Hearing disclosure process statement.

Lieutenant Commander Garcia.

LCDR GARCIA: Thank you, Dr. Talamini.

Both the Food and Drug Administration and the public believe in a transparent process for information gathering and decision making. To ensure such transparency at

the Open Public Hearing session of the Advisory Committee meeting, FDA believes that it is important to understand the context of an individual's presentation. For this reason, FDA encourages you, the Open Public Hearing speaker, at the beginning of your written or oral statement, to advise the Committee of any financial relationship that you may have with any company or group that may be affected by the topic of this meeting. For example, this financial information may include a company's or a group's payment for your travel, lodging, or other expenses in connection with your attendance at this meeting. Likewise, FDA encourages you, at the beginning of your statement, to advise the Committee if you do not have any such financial relationships. If you choose not to address this issue of financial relationships at the beginning of your statement, it will not preclude you from speaking.

Dr. Talamini.

DR. TALAMINI: Thank you, Lieutenant Commander Garcia.

There's been one formal request to speak today. Laura Gottschalk, Ph.D., will be speaking on behalf of the National Center for Health Research in Washington, D.C.

Dr. Gottschalk, we've got 10 minutes allotted.

DR. GOTTSCHALK: Good morning. Thank you for the opportunity to speak today. My name is Dr. Laura Gottschalk, and I received my Ph.D. in cellular and molecular medicine from the School of Medicine at Johns Hopkins, and I'm currently a senior fellow at the National Center for Health Research.

Our research center scrutinizes scientific and medical data and provides objective health information to patients, providers, and policymakers. We do not accept funding

from pharmaceutical companies, and therefore I have no conflicts of interest to disclose.

Our research center is very interested in the quality of medical care, and one of the first steps towards ensuring the safety of medical devices is correct classification. We agree with the FDA's recommendation to reclassify the urogynecologic surgical mesh instrumentation from Class I to Class II. We previously supported this up-classification of this instrumentation in a public comment to the FDA in July of 2014.

Currently, surgical mesh instrumentation is listed as a Class I device. Class I devices are subject only to general controls. They do not need to submit data to the FDA to ensure that this device is appropriately designed or manufactured. As a result, medical device reports have cited injuries associated with the instrumentation, such as organ perforation, blood loss, hemorrhaging, and numerous instances of the devices breaking and leaving fragments in patients. Clearly, Class I controls are insufficient for properly regulating this type of device. Therefore, we strongly support the up-classification to Class II with special controls. We specifically support the special controls suggested by the FDA, which are clear and proven in ensuring the safety and efficacy of the instrumentation.

We also agree with the FDA's suggestion that bench and/or cadaver testing can help ensure that surgical mesh instrumentation is appropriately designed and limits damage to blood vessels, nerves, connective tissue, and other structures. Testing the accuracy of this instrumentation is especially important because the operation to insert the surgical mesh is performed blind. Since the surgeon cannot directly see where he or she is placing the mesh, the precision of the instrument to correctly position the mesh is

paramount. The suggested up-classification and special controls of the mesh instrumentation would be a step in the right direction for the safety of all patients who undergo this surgical procedure.

We would also like to voice our support for improving the regulation of the centrifuge-type therapeutic apheresis device, product code LKN. As the Executive Summary describes, there have been a number of injuries as well as some deaths associated with the malfunction of the centrifuge apheresis devices as listed in the MAUDE database. The classification of these devices should accurately reflect the danger that they could pose to patients due to malfunction or misuse. In our view, since patients died when this device malfunctioned, it should be considered a Class III device.

However, if the FDA decides to instead designate it as a Class II device with special controls specific to the adverse events that are unique to centrifuge apheresis devices, the FDA needs to go the extra mile to ensure those controls are sufficient. We agree with the special controls suggested by the FDA to test the biocompatibility and performance as well as improve the labeling of the centrifuge devices. These special controls directly address problems that have been or could possibly be experienced while using the instruments.

Additionally, the suggested control of clinical performance testing would provide the FDA with valuable information pertaining to the performance and adverse events of the devices in a clinical setting. This information would strengthen the FDA's ability to properly regulate the devices in the future, as well as provide better information to clinicians and patients on the operability of these lifesaving devices.

In conclusion, there are a number of devices currently on the market that pose safety risks to the public because they were inappropriately designated as Class I. The up-classification of surgical mesh instrumentation from Class I to Class II as well as the new classification of centrifuge apheresis devices as Class II or III are both moves towards increasing patient safety. The special controls suggested by the FDA should be carefully evaluated to determine if they are adequate to protect patients from undue harm.

Thank you.

DR. TALAMINI: Thank you, Dr. Gottschalk.

Does anyone in the audience wish to additionally address the Panel? If so, we've got 3 minutes allotted for any other public speakers.

(No response.)

DR. TALAMINI: I don't see any, so we'll declare the public comment portion of this part of the meeting to be closed.

Does anyone on the Panel have a question for our public speaker today?

(No response.)

DR. TALAMINI: No? Okay.

DR. HICKS: Mark, I do. One quick one.

DR. TALAMINI: Oh. Dr. Hicks, a question.

DR. HICKS: Yeah. Could you give us a statistical kind of look at the number of perforations and vascular injuries that you all discovered in this, so we have some kind of point to look at?

DR. GOTTSCHALK: I'm sorry, I didn't look at that in detail. I looked into the deaths

that were associated with it in the MAUDE database. But beyond that, I didn't go into details looking at that.

DR. HICKS: But what I'm just saying, you just commented about the fact that the instrumentation, the mesh implant instrumentation, led to bleeding and perforation of the bowels. Do you have any data about the percentage of that? Is it high, low, or did it just happen once?

DR. GOTTSCHALK: That's a good question, and the data that I looked at were in the Executive Summary that was provided by the FDA. So I believe they have some numbers in there, but we didn't do any additional research on that ourselves.

DR. TALAMINI: And I think that will be part of the FDA's --

DR. GOTTSCHALK: Um-hum.

DR. TALAMINI: -- presentation, Dr. Hicks.

Any other questions from the Panel?

(No response.)

DR. TALAMINI: Okay. In that case, now we'll declare the public comment portion closed.

I'd like to take the temperature of the Panel. Is there an appetite for a break now, or would you rather press ahead? Press ahead, okay.

And is the FDA okay with pressing ahead?

DR. FISHER: Absolutely. Thank you.

DR. TALAMINI: Okay, all right. In that case, I would like to invite the FDA up to the podium to begin their presentation on the first topic. The presenter is Dr. Sharon

Andrews.

Dr. Andrews.

MS. ANDREWS: Good morning. My name is Sharon Andrews. I'm the Acting Branch Chief for the Obstetrics and Gynecology Devices Branch. Today I will be presenting on the FDA's proposal to reclassify urogynecologic surgical mesh instrumentation. For the remainder of this presentation I will use the term urogyn in place of urogynecologic.

The purpose of today's meeting is to obtain Panel recommendations regarding the reclassification of urogyn surgical mesh instrumentation from Class I to II. We are seeking Panel input on the risks to health and benefits of urogyn surgical mesh instrumentation, whether Class II is the appropriate regulatory class for these devices, and if the Panel determines that Class II is appropriate, what are the special controls that mitigate the risks to health?

During today's presentation, I will describe urogyn surgical mesh instrumentation and summarize their regulatory history. I'll discuss our review of the medical device report database and the published literature. Finally, I will discuss the risks to health and proposed mitigations we identified for these devices and our proposed reclassification and special controls.

So let's start with the device description. Urogyn surgical mesh instrumentation are designed for use during urogyn surgical mesh procedures. These devices do not include general instrumentation used during urogyn surgical mesh procedures. General instrumentation will remain in Class I.

Urogyn surgical mesh instrumentation aids in insertion, placement, fixation, and/or

anchoring of urogyn surgical mesh. It's typically composed of a stainless steel needle attached to a plastic handle. However, the design of the instrumentation is dependent upon the urogyn surgical mesh procedure in which it is used.

Urogyn surgical mesh procedures are intended to treat pelvic organ prolapse, or POP, and female stress urinary incontinence, or SUI. POP procedures include transvaginal and abdominal repair. The latter is referred to as the sacrocolpopexy. Female SUI procedures include placement of retropubic slings, transobturator slings, and mini-slings.

This slide provides examples of different urogyn surgical mesh instrumentation. The image on the left-hand side is of the Capio needle. This device is used during transvaginal POP procedures. The next two images depict instruments used during female SUI procedures. The middle image is of retropubic sling needles, and the image on the right is of transobturator sling needles.

These images display how the instrumentation is used to place urogyn surgical mesh. The image on the left depicts placement of a retropubic sling. The needle is placed through an incision in the anterior vaginal wall. It passes behind the pubic bone and penetrates through the abdominal wall. The image on the right depicts placement of a transobturator sling. The needle is placed through an incision in the anterior vaginal wall, passes through the obturator foramen, and penetrates through the upper thigh or groin.

And what you can see from those images is that implantation of urogyn surgical mesh is a complex procedure. It's performed blind, and it relies on the instrumentation, palpation of anatomic landmarks, and experience to access critical ligaments and attach anchors or other devices needed to secure the mesh. In short, without appropriately

designed instrumentation, the surgeon will not be able to correctly place and secure the mesh.

Urogyn surgical mesh instrumentation can broadly be placed into one of three categories. The first category consists of instrumentation that is designed, packaged, and indicated for use with one specific urogyn surgical mesh device. This packaged combination is often referred to as a urogyn surgical mesh kit. The retropubic and transobturator sling needles shown in one of the previous slides falls under this category.

The second category includes instrumentation designed and indicated for use with multiple urogyn surgical mesh devices. The instrumentation is packaged and marketed separately from the mesh devices. Oftentimes, this type of instrumentation is multi-patient reusable.

The third category includes instrumentation designed and indicated for use with a urogyn surgical mesh device but also indicated for non-mesh urogyn procedures, for example, pelvic floor repair procedures. The Capio needle shown in one of the previous slides falls into this category.

Next, we'll discuss the regulatory history of urogyn surgical mesh. As discussed during this morning's presentation, medical devices are classified into one of three classes based on the risks to health, with Class I being the lowest risk category and Class III being the highest risk category. Our available regulatory controls increase with each subsequent class.

Urogyn surgical mesh are Class II or Class III devices. We recently reclassified surgical mesh for transvaginal POP repair to Class III. All other urogyn surgical mesh

devices are Class II devices.

Urogyn surgical mesh instrumentation are Class I devices. They are currently regulated under two separate regulations, 21 C.F.R. 876.4730 for manual gastroenterology-urology surgical instrument and accessories, and 21 C.F.R. 878.4800 for manual surgical instrument for general use.

Currently, urogyn surgical mesh instrumentation are exempt from premarket notification, or 510(k), submissions. This means that the FDA does not review their design, biocompatibility, sterilization method, labeling, etc., prior to marketing. For urogyn surgical mesh kits, we have reviewed the instrumentation in the premarket notification, or 510(k), submitted for the urogyn surgical mesh. However, we are limited with respect to the type and amount of information we can request specifically on the instrumentation because they are Class I devices. The proposed reclassification of these devices to Cass II would subject them to special controls and premarket notification.

Section 513 of the Food, Drug, and Cosmetic Act outlines three steps to reclassify a medical device. The first step is publication of a proposed order in the *Federal Register*. In the proposed order, the FDA outlines its rationale for the proposed reclassification. The second step is consideration of comments to a public docket. This allows outside stakeholders to provide their input on the proposed reclassification. The third step is a meeting of a device reclassification panel, just what we are holding today. And the fourth and final step is publication of a final order.

Regarding the first step of the reclassification process, we published a proposed order on May 1st, 2014. This order proposed to reclassify surgical mesh indicated for

transvaginal POP repair from Class II to Class III and urogyn surgical mesh instrumentation from Class I to Class II.

We finalized the reclassification of surgical mesh indicated for transvaginal POP repair from Class II to Class III on January 5th, 2016. That was based on input from the OB/GYN Medical Devices Panel on September 8th, 2011.

Regarding the second step of the reclassification process, we received 13 comments to the public docket for the proposed order pertaining to the reclassification of urogyn surgical mesh instrumentation. We received six comments from patients who supported the reclassification to Class II or to Class III. We received one comment from a consumer group which requested the instrumentation have the same classification as the surgical mesh with which it is intended to be used. We received three comments from consumer groups that supported the reclassification to Class II. We received two comments from clinical organizations that supported the reclassification to Class II. And we received one comment from industry, which did not support the reclassification and stated that the FDA did not provide valid scientific evidence to support the proposal.

So to support our proposed reclassification of urogyn surgical mesh instrumentation, we reviewed both the MDR database and the published literature. So, first, I'll summarize our review of the MDR database.

MDRs are used to monitor device performance, detect potential device-related safety issues, and contribute to the benefit-risk assessment of medical devices. Manufacturers, importers, and device user facilities are required to report known adverse events. MDRs provide a qualitative snapshot of adverse events for a specific device or

device type when used in a real-world environment. However, the MDR database is a passive surveillance system, and MDRs can contain incomplete, inaccurate, untimely, unverified, or biased data.

To identify the MDRs associated with urogyn surgical mesh instrumentation, we searched the MDR database for all MDRs reported from January 1st, 2008 to December 2nd, 2015, using surgical mesh product codes. Product codes are three-letter codes that are used to categorize device types. There can be multiple product codes associated with a particular device. However, in the MDR database, device reports are placed under a primary product code.

We filtered the search terms based on terms specific to instrumentation and then we identified MDRs associated with the intraoperative placement of urogyn surgical mesh and related to the instrumentation.

Our MDR search yielded 463 MDRs; 438 were submitted by manufacturers, 14 were submitted by a user facility, and 11 were voluntary reports. The event types included 339 malfunctions and 124 injuries.

This table summarizes the MDRs received per product code. This table includes two general surgical mesh product codes, FTL and FTM. We used these two product codes before urogyn surgical mesh-specific product codes were implemented in 2012. However, the MDRs included under FTL and FTM here apply only to urogyn surgical mesh. We received the most MDRs for instrumentation used during transvaginal POP procedures.

This table summarizes the most frequent patient problem codes noted in the MDRs for urogyn surgical mesh instrumentation. A single MDR may include more than one

patient problem code. We highlighted the problem codes of interest in yellow. Most MDRs had no known impact or consequence to the patient. However, we also received numerous MDR reports related to the instrumentation breaking during use and leaving device fragments in the patient. In addition, we received reports of perforation and blood loss or hemorrhage.

You'll note that the perforation and blood loss problem codes have low numbers of MDRs associated with them. Based on our review of the published literature, we believe these numbers are an underestimation of the patient problems associated with urogyn mesh instrumentation.

This table summarizes the most frequent device problem codes. A single MDR may include more than one device problem code. The vast majority of reports are related to the instrumentation detaching or breaking. There were also a number of reports related to difficulty using the instrumentation.

This table summarizes the most common manufacturer conclusions for the MDRs received. The manufacturer conclusion is a required part of the MDR report. In the vast majority of cases, the manufacturer was unable to draw a conclusion because the device was not returned, because they were unable to confirm the complaint, or because an evaluation was in progress. Therefore, as noted on a previous slide, although most MDRs did not have an impact or consequence to the patient, there is a lack of information to determine causality.

Based on the MDR review, we concluded that the failures of urogyn surgical mesh instrumentation occur, and that these failures have the potential to adversely affect

patients. Specifically, we noted numerous reports related to the devices breaking during use, leaving fragments in the patient, and difficulty with use. We believe these data support the need for well-designed instrumentation and that instrumentation should be evaluated premarket to help ensure adequate performance, specifications, and labeling.

In addition to reviewing the MDR database, we reviewed the published literature. To complete the literature review, we searched the PubMed and Embase databases using terms related to adverse events, type of urogyn condition, type of surgical instrumentation, study design, device name, and manufacturer name. We limited references to those that evaluated human subjects, were written in English, and were published between 1997 and 2015. We excluded references that evaluated male subjects, included only information on non-primary procedures, and did not discuss intraoperative and perioperative adverse events, included previously published data already included in the literature review, or were case reports or review articles. This resulted in 207 references for review.

This slide summarizes the number of references included in the search pertaining to each urogyn surgical mesh procedure. The majority of references described SUI procedures.

We extracted data from the published literature for three major categories of adverse events related to urogyn surgical mesh instrumentation: organ perforation and injury; vascular injury and bleeding; and nerve injury and pain

We believe these adverse events could reasonably be assumed to be related to the instrumentation and not the surgical mesh.

Although it was not the focus of our literature review, we do want to note that the adverse events noted on this slide can have significant clinical sequelae, including chronic pain, infection, the need for additional surgical procedures, and potentially death.

Organ perforation and injury include adverse events captured in the literature as organ perforation, organ injury, urethral injury, ureteral injury, bladder injury, bladder perforation, rectal injury, cystotomy, and enterotomy. For retropubic procedures, 54 out of 74 references reported rates of up to 23.8%. For transobturator procedures, 25 out of 65 references reported rates of up to 5.8%. For mini-sling procedures, 6 out of 32 references reported rates of up to 2.6%. For transvaginal repair procedures, 16 out of 33 references reported rates of up to 13.1%. And for abdominal repair procedures, 1 reference reported a rate of 3.6%.

Vascular injury and bleeding include adverse events reported in the literature as hemorrhage, vascular injury, hematoma, and blood transfusion. For retropubic procedures, 38 out of 74 references reported rates of up to 29.4%. For transobturator procedures, 19 out of 65 references reported rates of up to 11.9%. For mini-sling procedures, 6 out of 32 references reported rates of up to 20.5%. For transvaginal repair procedures, 15 out of 33 references reported rates of up to 7.7%. And for abdominal repair procedures, 1 reference reported a rate of 2.8%.

Nerve injury and pain events include adverse events reported in the literature as nerve injury, nerve damage, leg pain, thigh pain, buttock pain, and neurological symptoms. For retropubic procedures, 5 out of 74 references reported rates of up to 5.3%. For transobturator procedures, 11 out of 65 references reported rates of up to

30.8%. For mini-sling procedures, 5 out of 32 references reported rates of up to 4.1%. For transvaginal repair procedures, 15 out of 33 references reported rates of up to 39.1%. And for abdominal repair procedures, 1 reference reported a rate -- 1 out of 3 references reported a rate of 14.9%.

Overall, we believe that the published literature demonstrate that adverse events can occur as a result of urogyn surgical mesh instrumentation and at potentially high rates. We believe these data support the need for well-designed instrumentation evaluated premarket to ensure adequate performance, specifications, and labeling. More specifically, we believe we should review design aspects such as the curvature of the needles and the dimensions of the needles, with the option to review the ability of the instrumentation to traverse complex anatomy in a blind fashion either through pelvic models on the bench or through cadaver testing.

Based on our review of the MDR database and the published literature, we identified risks to health associated with urogyn surgical mesh instrumentation and proposed mitigations for those risks.

In the May 1st, 2014 proposed order, we identified the following risks to health associated with urogyn surgical mesh instrumentation. The first risk was perioperative risks, which include organ perforation or injury and bleeding, including hemorrhage and hematoma. The second risk was damage to blood vessels, nerves, connective tissue, and other structures. This may be caused by improperly designed and/or misused surgical mesh instrumentation. Clinical sequelae include pelvic pain and neuromuscular problems. The third risk is adverse tissue reaction. This may be caused by non-biocompatible

materials. And the fourth risk is infection. This may be due to inadequate sterilization and/or reprocessing instructions or procedures.

Please note that the adverse events of adverse tissue reaction and infection are general risks that apply to medical devices that are patient contacting. Therefore, as with other such medical devices, it's challenging to find explicit information in the MDRs and the published literature specific to those risks to health. You'll note that the data from the MDR database and the published literature primarily support the first two risks. However, we would emphasize that mitigating the last two risks is critical to support the safety and effectiveness of these devices.

We're seeking the Panel's input on the identified risks to health for urogyn surgical mesh instrumentation. The Panel should assess whether this list completely and accurately identifies the risks to health presented by urogynecologic surgical mesh instrumentation and whether any other risks should be included in the overall risk assessment of the device type.

This table provides the proposed mitigations for each identified risk to health. Please note that per the footnotes, items in this table have been revised from the proposed order.

For the risk of perioperative injury, we propose that nonclinical performance testing, labeling, and shelf life testing would mitigate that risk. For damage to blood vessels, nerves, connective tissue, and other structures, we propose that nonclinical performance testing, labeling, and shelf life testing would mitigate that risk. For adverse tissue reaction, we propose biocompatibility testing to mitigate that risk. And for

infection, we propose sterilization validation, reprocessing validation, shelf life testing, and labeling to mitigate that risk.

We'll now move on to our proposed classification and special controls. We have determined that valid scientific evidence demonstrates that special controls, in addition to general controls, are necessary to provide a reasonable assurance of the safety and effectiveness for urogyn surgical mesh instrumentation. Accordingly, we believe that urogyn surgical mesh instrumentation should be reclassified from Class I to Class II (special controls).

We're seeking Panel input on whether urogyn surgical mesh instrumentation should be reclassified from Class I. The Panel should assess whether general controls alone or the combination of general and special controls provide reasonable assurance of safety and effectiveness of urogyn surgical mesh instrumentation.

We believe that the following special controls, in addition to general controls, are sufficient to mitigate the risks to health attributable to urogyn surgical mesh instrumentation.

- The device must be demonstrated to be biocompatible.
- The device must be demonstrated to be sterile, including adequate reprocessing for reusable devices.
- Performance data must support the shelf life of the device by demonstrating package integrity and device functionality over the requested shelf life.
- Nonclinical performance testing must demonstrate that the device meets all

design specifications and performance requirements, and that the device performs as intended under anticipated conditions of use. And

- Labeling must include:
  - Information regarding the mesh design that may be used with the device;
  - Detailed summary of the clinical evaluations pertinent to use of the device;
  - Expiration date; and
  - Where components are intended to be sterilized by the user prior to initial use and/or are reusable, validated methods and instructions for sterilization and/or reprocessing of any reusable components.

If the Panel finds that Class II regulatory controls are needed to provide a reasonable assurance of the safety and effectiveness of urogyn surgical mesh instrumentation, we're seeking Panel input on the proposed special controls for these devices. The Panel should assess whether the identified special controls appropriately mitigate the identified risks to health and whether additional or different special controls are needed.

We're proposing to develop a regulation for urogyn surgical mesh instrumentation under Part 884, Obstetrical and Gynecological Devices. This regulation would be titled specialized surgical instrumentation for use with urogyn surgical mesh. This regulation would be identified as follows:

Surgical instrumentation for use with surgical mesh for urogynecologic procedures

is a prescription device used to aid in insertion, placement, fixation, or anchoring of surgical mesh for procedures including transvaginal pelvic organ prolapse repair, sacrocolpopexy (transabdominal pelvic organ prolapse repair), and treatment of female stress urinary incontinence. Examples of such surgical instrumentation include needle passers and trocars, needle guides, fixation tools, and tissue anchors. This device does not include manual gastroenterology-urology surgical instrument and accessories nor manual surgical instrument for general use.

The special controls cited in the regulation would be as stated previously, so I'll not read through the items on this slide.

In conclusion, we propose that urogyn surgical mesh instrumentation are reclassified from Class I to Class II with special controls and be subject to premarket notification requirements. We also recommend a new regulation for these devices under Part 884, Obstetrical and Gynecological Devices.

I would like to acknowledge the following individuals in the Office of Device Evaluation and the Office of Surveillance and Biometrics for their help in developing this presentation and the FDA Executive Summary.

Thank you.

DR. TALAMINI: Thank you very much for that very clear presentation.

It's time for clarifying questions from the Panel. I have a clarifying question. As I understand it, parallel devices in general surgery, thoracic surgery, that might be similar to these that are already Class II devices with special controls; is that true?

MS. ANDREWS: I think that if you look across the devices that we regulate and

medical devices that are used to place other medical devices, there's, I think, a range in how they're classified. Some are Class I, some are Class II, some are Class III. I think it just depends on the instrumentation itself. For the urogyn surgical mesh instrumentation, we believe that the risks that we have identified, they can be mitigated through both general and special controls. So we think that Class II is appropriate for these devices specifically.

DR. TALAMINI: Clarification questions from the Panel?

Yes, Dr. Iglesia.

DR. IGLESIA: Cheryl Iglesia.

Thank you so much for your view. So I have some concerns with the data that was presented. You know, the MDR is very limited, and the problem with that, even at 463 reported instances of a complication with an instrument, the denominator is huge. When we look at the number of prolapse cases, that is far less than the number of stress incontinence cases that are performed annually here in the United States and worldwide, and we probably have data on millions of patients who've actually been implanted with the sling meshes. And I personally have done 2,000.

So the issue with the sling mesh and the instrumentation here is the majority of those that you classified as having a malfunction did not have significant harm. And the harm that's presented -- and it's horrific harm when you hit a bowel injury unrecognized and the patient dies from that, or a big vascular artery and you lose a leg or have massive transfusion. I understand that. But in the right hands and in the right patients, that should not happen, and that's not the instrument. I can tell you that with high-volume surgeons, that's a surgical error.

And I don't think we can put that big organ injury and that big vascular injury -- this is the part where I know we don't control the practice of medicine, you guys don't, but that's where we got to be really good with the training and introduction of this stuff. So the denominator matters and the surgeon matters, and in the right hands, it's not the instrument.

While I agree that the biocompatibility, the sterility, the infection, and the fact that the instruments can't break off is very important, and for that reason I'm going to support probably the up-classification, I'm a little bit concerned about the precedent that that may set in terms of the availability of the current devices that are in place. If we do that, I do not want that to impact the ability for women to have slings. You know, I think that it's not the sling and it's not the instrument.

For that reason, I think it's going to be the minority where there is an issue, but I -- you know, where something -- the instrument actually breaks. The instruments have to stay in the person. The instrument is something to introduce, and some of them are disposable, and some of them are reusable, and I think that that process needs to be -- have some special controls on it.

But I really think we have to be careful about this little numerator and maybe some significant outliers, because those -- even the complication rates when you're in the double digits and how we should all be under the zero, you know, less than 0.05% for that. So that's my two cents.

DR. TALAMINI: A response? Again, we're sort of in the clarification question phase. I think we'll get into a lot more of this when we deliberate, but a response to that

in terms of clarification.

MS. ANDREWS: So I think what I would say is we certainly acknowledge that there is a component of the user that affects, you know, these adverse events, and I don't think that we are trying to say that by implementing these special controls, that we can eliminate all of these adverse events, because some of them are just very much tied to the user and their training. What we're hoping to do is that, through this reclassification, we will be able to look at the design of these instruments and some of this other preclinical testing premarket. And we're hopeful that by doing that, we can perhaps minimize some of them and improve the design of them.

DR. TALAMINI: So I have a second clarification question. This will also enable the FDA to have a more robust data collection regarding all aspects of use of these devices, yes?

MS. ANDREWS: It will, because we'll see that data premarket. So it's not just the preclinical testing, but if there is data out there on use of the instrumentation, we'll be able to look at that premarket. That may help us inform the labeling.

DR. TALAMINI: Other clarification questions?

Dr. Martens.

DR. MARTENS: Yes, thank you. I definitely agree with what Dr. Iglesia had to say a little bit. I don't think it's the FDA responsibility to make sure the devices are used properly. It's there to make sure they're safe and effective. It's my job to make sure my surgeons are certified and properly trained to use the device and to monitor their use in case they have an increased complication rate.

However, I am a little concerned that you didn't include a clinical component. You had nonclinical testing. In my examples and I wanted to -- my question to you is why didn't you include clinical testing? I've been involved with several new devices where modifications were made, especially in a large field of devices like this, that try to improve either on the ease of use or the cost. The cost aspect you touched on. There will be new materials that aren't as durable and there will be fragmentation. But devices I know in the IDEs, they tried to make it a smaller narrow tip in order to facilitate ease of entry, and what they did is increase the perforation rate. I can see, unless you have very specific controls over the degree of arc or angle of use, that in an experienced surgeon who's done several thousand, if they change the degree 5% because they think it feels better to the surgeon, you then put yourself in a realm of injuring more vessels. And so I'd like to have strict controls over that and perhaps some clinical testing, because what works well on a cadaver or a model, when you try to use that, push that tissue in, the force you need may cause you to cause more injury. So I think I would recommend or ask you, why didn't you include clinical testing?

MS. ANDREWS: So I think we're hoping to get some of that information through testing in a pelvic model or through cadaver testing. We did think about including clinical testing specifically as a special control for the instrumentation. However, we felt that that would probably be more applicable to the mesh.

DR. TALAMINI: Dr. Fisher, did you have a question or a comment?

DR. FISHER: I think Sharon just answered it. But the one thing that we did was we tried to be as careful as possible to -- when we went through the MDRs, to look at reports

that were specific to the instrumentation. And what that did allow us to do was to pull out signals about the fragmentation and the breaking of the instruments. So that's what we were -- you know, those are the things that we were specifically going after for the instrumentation because, right now, if we ask for mechanical testing, a sponsor can push back and say you know, it's a Class I device. We don't have to do that. So moving this up to Class II would allow us to see that mechanical performance testing.

Sharon was point on. You know, we did consider a clinical training element for the instrumentation where we thought that that would be more appropriate was to actually put it in with the mesh itself. So actually the placement, you know, the utilization of the instrumentation with the placement of the mesh, that's where we were actually looking for the clinical data, and we felt that, well, like Sharon said, the nonclinical, either the bench testing, in vivo, possibly in vivo models or cadaver testing would be sufficient for the instrumentation by itself.

DR. TALAMINI: So, again, by way of process, we're going -- this is different from yesterday, for those of you who were on the Panel yesterday. Yeah, I'll get to you. Our goal right now is to clarify what has been presented, and then we're going to discuss amongst ourselves, as experts, what our feelings are, pro, con, include, don't include. The FDA has put forth a proposal to go from Class I to Class II with special controls. We want to be as clear as we can on what they've said.

So with that in mind, yes, Dr. Carson.

DR. CARSON: Your proposed mitigations for the mesh includes some mitigations for adverse tissue reaction and infection. But I didn't see those adverse reactions

reported in your previous information. So I'm curious why you're -- is there something that you didn't include about rejection or infection, or why would you recommend that mitigation if it's not an issue?

MS. ANDREWS: Sure. So the data in the MDRs and the published literature primarily relate to the first two risks that we identified. But regarding adverse tissue reaction and infection, we see those as general device risks that apply to any device that's patient-contacting that needs to be sterile. And I think that because of that, it's going to be difficult to find explicit information in the published literature or the MDRs that points to, you know, there's this adverse event that occurred because the device material is not biocompatible. And so the argument we're trying to make is that for a device that's patient-contacting, we need to use biocompatible materials, because if we don't, you could have an adverse tissue reaction, and biocompatibility testing is the way to mitigate that. So the same thing with infection. A device needs to be sterile in order to be used safely. We want to make sure that we're doing the appropriate sterilization validation, reprocessing validation.

DR. CARSON: So are these mitigations used for all implantable devices?

MS. ANDREWS: So for any implantable devices, we would expect to see biocompatibility testing. The amount of biocompatibility testing we expect premarket depends upon the type and the contact duration of an individual device. The same thing with any device that needs to be sterile. We would expect to see sterilization validation premarket. If a device is intended to be reprocessed, we would expect to see reprocessing validation.

DR. TALAMINI: But if I understand, to make Dr. Fisher's point again, if it's a Class I device, there can be pushback on even those issues, correct?

DR. FISHER: Currently, that is correct.

DR. TALAMINI: Other clarification?

Dr. Donatucci.

DR. DONATUCCI: Before I left practice 4 years ago, there was a male sling that was essentially the same device, the same obturator, the same attachment of the sling to the needle. I don't know whether it's still marketed because, again, I'm not practicing any longer. But my question would be if it is, why is that not also being considered for -- is there a difference between -- solely on gender, would the instrument for men still remain Class I and only women would be Class II?

MS. ANDREWS: So what I will say is oftentimes the instrumentation is packaged with the mesh in a kit, and when we review the premarket notification for that surgical mesh kit, we will ask for information regarding the instrumentation. So it can be covered that way, but what we are trying to do is -- you know, there are instruments that are not packaged with the mesh. And as I mentioned, there have been instances where we ask for premarket information on instrumentation, and we get pushback because they're Class I devices. I would say the same concerns are probably applicable to a male sling, but the scope of what we're proposing today is sort of limited to the female indications for POP and SUI.

DR. DONATUCCI: Again, I just have to -- you know, I would say, having gone through the training and actually done some of those procedures, the risks are absolutely

the same, except you're not going to injure the vagina. But bowel injury, nerve injury, vascular injury are all the same. So I don't understand why we wouldn't classify the ones used in males also as Class II.

DR. TALAMINI: That's a good question.

Dr. Fisher.

DR. FISHER: So, Dr. Andrews pointed out, in her presentation, that the instrumentation comes kind of in three different buckets. It can be packaged with the mesh. It can be used repeatedly so that you can purchase it individually and use it with mesh. And then there is instrumentation that could be used for a variety of different procedures. So what we're looking to do here is to classify all the instrumentation under one regulation -- excuse me, under one classification. So it would really depend on how it was labeled. So, right now, if that instrumentation was to include a labeling for urogyn mesh implantation, then we would be looking for that type of -- we would be looking for the types of information that Dr. Andrews pointed out.

DR. TALAMINI: Dr. Iglesia.

DR. IGLESIA: I just have another question about -- Cheryl Iglesia. If these do get reclassified, and I understand that the current devices will remain on the market and the manufacturers have to provide either the 510(k) or PMA evidence to support safety, I just want to make sure how -- will that have a clinical impact in the sense that -- I don't know if somebody doesn't have it, but what kind of clinical impact should I expect? I want to do a sling and also be able to do it. The patient needs a certain --

MS. ANDREWS: So we are not anticipating a clinical impact, and we're not

anticipating any changes in the availability of these devices. We expect that this type of testing is -- are things that the manufacturers have probably already done or should've already done as part of their design validation of the instruments. So we expect that they should be able to put the information together pretty quickly and send that in to us.

DR. IGLESIA: And then, as you up-classify the instrument, the device itself remains 510(k) for the slings and the sacrocolpopexy mesh, that PMA Class III for the transvaginal mesh.

MS. ANDREWS: Yes.

DR. IGLESIA: And so actually moving forward the PMA, those studies that are being done probably will have information on the instruments involved, correct?

MS. ANDREWS: Yes, that's true.

DR. IGLESIA: Okay. So that's two for one.

MS. ANDREWS: Um-hum.

DR. IGLESIA: And I just really am really concerned about -- since I feel that a lot of this data is really scary, but I think that the percent is really small because the genre is so huge, I'm just really concerned about the impact that we would have for those of us in practice and women who would obviously benefit from this.

MS. ANDREWS: And that's important to us, too, and we do want to make sure that these instruments remain available for the surgeons who need to use them, and that's definitely going to be part of our considerations moving forward.

DR. TALAMINI: Dr. Fisher.

DR. FISHER: I'd like to add that right now, with surgical mesh being in two, any of

the instrumentation that comes with surgical mesh, we would be -- we would already be asking for this information. Even with the up-classification, we would have an opportunity to look at this information, and I don't think it's going to be overly burdensome to the sponsors. Like Dr. Inge just pointed out, you know, this is something that they should have already looked at. So it's more of us being able to evaluate that information.

DR. TALAMINI: Yes, Dr. Fennal.

DR. FENNAL: Mildred Fennal.

I just want to ask FDA a question for clarity for my reasoning. This instrument that we're talking about, it does present risks for injury to the person. So my question is, was classification at Class III not considered because it was not thought that the potential risk was unreasonable and we just went with Class II, that everything could be accomplished with that? It's not unreasonable, so you didn't go to Class III? Is that --

DR. FISHER: So one of the things that Marjorie Shulman presented this morning is that we take that into consideration. What we look at in this situation is we try to identify the risks, and we'll be asking the Panel, have we identified all the risks? And then can we put special controls in place to mitigate those risks? And we're going to talk about the special controls that we're putting in place. And if the special controls are not adequate to address those risks, that's when you start taking into consideration as to if it should go to Class III.

So part of the deliberation and the discussion is going to be have we identified all the risks, and are we going to be able to mitigate those risks with the special controls that we are proposing putting in place? And, you know, we just have to remember that as of

right now, we have been regulating these surgical instrumentations as Class I for years.

DR. TALAMINI: So do all the Panel members have written in front of them the specific FDA questions? You do, okay. So what I would -- if there are no other clarification questions, we can thank Dr. Shulman, and I'd love to move to a discussion among the Panel.

So thank you, Dr. Shulman. I'd like to --

(Off microphone comment.)

DR. TALAMINI: Oh, I'm sorry, Dr. Andrews. I'd like to move to a discussion among the Panel members focused a little bit on these, on the questions as you see them in front of you, prior to actually directly addressing those questions.

So one question that has been raised is whether all of the risks that should be addressed have been addressed. And I think if you are looking at the specific questions that will be asked, it's perioperative risk, organ perforation or injury of bleeding, damage to blood vessels, adverse tissue reaction, infection.

From the Panel's point of view, has the FDA left anything out in terms of substantive risk with respect to these placement devices?

Dr. Iglesia?

DR. IGLESIA: Cheryl Iglesia.

So, again, I mean, I do understand that the arc and when you do the biocompatibility testing and modeling, you want to make sure that things are going in the right direction. I don't believe that these procedures are completely blind in the appropriate hands because you have haptic feedback against the bone. But in the wrong

hands, that's really bad. They shouldn't be placing these in.

And so at the top, (a) and (b) are perioperative risk or organ perforation, hematoma and damage. There's a part that you can't control, even despite with the best designs, with poorly trained surgeons. I think more focusing on adverse tissue reaction, infection, and maybe the fragmentation of the device, you know, falling apart; and the release mechanism, how the suture releases from the needle driver component, say, on a catheter device, which is not necessarily attached to mesh because that can also be used for tissue repair; but also how the plastic sheaths release, because I think some of the foreign body things you're having is the fact that the plastic remains and people don't recognize this. I mean, I pull it out to make sure that that plastic was designed to keep the mesh clean and not touching. A lot of stuff can remain. And I think that there have been case reports of that. So that kind of can be added. That's not an instrument, though. That's like covering the mesh, but it's attached, how it attaches to the instrument. Does that make sense?

DR. TALAMINI: Dr. Carson.

DR. CARSON: Yes. I want to just reiterate that I'm having a little bit of a problem understanding how the perioperative risk, organ perforation, and damage to anatomical structures are related to the device itself and especially the mesh itself.

DR. TALAMINI: So just in terms of a Panel response, you know, you can imagine one device might be 2 cm wide and blunt with -- you know, and another would be very sharp and very small, and they'd be different in the amount of damage they could potentially create in passing through the tissues, but I think your point is that it's mostly

the surgeon skill. But the instrument design itself would seem to obviously play at least some role, what the curvature is and all of those kinds of things.

Dr. Efron.

DR. EFRON: Yeah. I mean, I was going to say the same thing you did, Dr. Talamini, that I would equate it to doing a laparoscopic procedure and the difference between placing blunt trocars or sharp trocars. There is an increased perhaps incidence in sharp trocars of perforation of vessels and bowel, and you shouldn't have any of it if you're an adequate user. But there is an increased risk with a sharp trocar as opposed to a blunt trocar. So the actual device itself, how it's designed, how it's manufactured, and how it's put together would, I would imagine, play perhaps a role in these injuries.

DR. TALAMINI: Yes, Dr. Carson.

DR. CARSON: So could you answer that same thing for the mesh? I mean the instruments, I get it, but for the mesh?

DR. EFRON: We're not talking about the mesh, right? We're just talking about the instruments. We're not talking about the mesh. The mesh is a separate product. We're talking about the instrument used to implant the mesh.

DR. TALAMINI: So what I'm wondering, and I almost hate to say this, is whether Dr. Iglesia would push for inadequate training to be on the risk list for the special controls. But I imagine that's a step that is extreme and different from what the FDA is proposing.

DR. IGLESIA: Yeah. This is Cheryl Iglesia.

I clearly have a bias since we have a fellowship program. I've been a fellowship director. We've trained, you know, many residents and fellows on this device, and there

is a significant learning curve. And that's why I'm like, you know, one thing, when a patient goes to -- when you see a surgeon, the first thing that you're asked, you know, how many have you done? You know, what's your experience? Because high-volume surgeons, it's very different from someone who's doing 10 a week, like we do, each or something versus someone who's doing, you know, one or two a year.

DR. TALAMINI: Dr. Efron.

DR. EFRON: Again, that goes to credentialing, and that's really the hospital's responsibility or the organization's responsibility. It's not the responsibility, I don't think, of the FDA.

DR. TALAMINI: Dr. Donatucci.

DR. DONATUCCI: If I understand it, the needle that's passed then attaches to the mesh -- I think the device we saw yesterday is an example of that -- and locks. There can be failure of the locking mechanism, and the mesh can separate in the wrong place. So it's not quite analogous to placing a sharp or a blunt needle because you're going to use that transobturator needle to attach the mesh to it and then pull it through.

DR. EFRON: So is that a failure of the mesh, or is that a failure of the needle and the device? I mean, I guess what I'm saying is that the device itself has an attachment that the mesh gets secured to, correct?

DR. DONATUCCI: Yeah. Well, I mean, that's the argument of why it has to be Class II.

DR. EFRON: Right, right. I mean --

DR. DONATUCCI: I'm arguing for it, not against it.

DR. EFRON: Okay, okay.

DR. TALAMINI: So let's spend a little bit of deliberating time on that more general issue of Class I, Class II, Class III, since that question is going to be specifically asked. Are there Panel members that want to make a case, as we're deliberating now, for this remaining Class I?

(No response.)

DR. TALAMINI: Are there Panel members that want to make a case for this being a Class III device? Because there are aspects of that we haven't specifically discussed, other than the presentation this morning.

DR. MARTENS: I'm not advocating that. I have a question for the FDA. So once the classification is done and the manufacturers comply, any Type I -- Class I, II, or III could become the predicate device for future devices, or do you have to be at least a Class II?

DR. TALAMINI: Dr. Fisher.

DR. FISHER: So I'm not quite sure that I understand the question, but it sounds like could a Class I device be a predicate for future devices?

DR. MARTENS: Right, right.

DR. FISHER: It could be, but we would still be requiring certain data to show that it is substantially equivalent to that predicate. So that's one of the things that we do in the world of 510(k)s and Class II devices.

DR. MARTENS: But the Class I device wouldn't be subject to the increased controls, right?

DR. FISHER: If this goes to a Class -- if these devices are put into Class II, we will be

asking for 510(k)s for the devices that are currently in Class I by themselves.

DR. MARTENS: Right. And so what I don't want to happen is that we allow future devices that come that are based on the current devices and we haven't properly vetted the current devices. And when it happens, you know, the concept of the devices is a predicate device, everybody looks to be non-significantly different than that device, but it's five times less effective than that other device. So, you know, you can't go back and reclassify unless you have more significant data. So I just want to make sure. I mean, no one's looking at it for Class I, but Class II with the 510(k)s, there will be adequate review to make sure we have a safe predicate device for future devices to look on.

DR. FISHER: That's what we're hoping.

DR. MARTENS: Okay.

DR. TALAMINI: So then given that the Panel seems to be settling on this being a Class II device, there's the issue of Class II device with special controls or Class II device without special controls. Is there anybody that wants to argue for this device being Class II without special controls based on what you've heard or your experience?

(No response.)

DR. TALAMINI: So then we get to the issue of what those special controls should be, and we had a little bit of that discussion already.

Dr. Carson.

DR. CARSON: So before we go into it, that's a little bit of where I'm a bit unclear about. We heard that these are packaged sometimes with the mesh and the instrument. And so in those that are packaged with the mesh and the instrument, if there's -- that was

my question to Dr. Efron. The controls would apply to only the instrument even though it's packaged with the mesh; is that correct?

DR. FISHER: So for mesh that is packaged -- excuse me, with instrumentation that is packaged with the mesh, as of right now, the mesh is in Class II -- excuse me, it was a couple weeks ago, but now it's being up-classified to Class III. If the --

(Off microphone comment.)

DR. FISHER: Excuse me. Yes, thank you very much. When they're packaged together like that, that gives us the ability to ask for this additional information. Okay, so the biocompatibility, the mechanical testing, all of the things that we're putting on the table for consideration, when it's packaged with the mesh, we're able to get that because of the classification of the mesh and the way that the instrumentation is with that mesh. Okay, so the way it's packaged together, if the instrumentation is sold separately, which you can purchase it separately --

DR. CARSON: Um-hum.

DR. FISHER: -- then it's not tied to the mesh. So that's where we start getting some pushback from industry because they're Class I by themselves, and they say, hey, this is a Class I device. It's the instrumentation. And so what we're saying is we appreciate that. Based on some of the risks that we've identified, we think that for the instrumentation by itself, that we would still like to see some additional information.

DR. TALAMINI: And, in reality, there are three possibilities here, right? It can be a disposable instrument packaged with the mesh. It can be a disposable instrument not packaged with the mesh. Or it can be a reusable or permanent instrument unrelated to

the mesh but designed for this purpose, correct? All three of those would fall into this.

So we're to the concept of special controls, and you can see, in the questions, the second page of the questions, the FDA also is asking us about sort of three different assessments regarding life-supporting/life-sustaining issues, potential or unreasonable risk of injury, and whether sufficient information exists to establish special controls. You can see those in (b), (c), and (d) of that question. Do you have thoughts regarding those?

Dr. Iglesia.

DR. IGLESIA: Cheryl Iglesia.

I think these are general controls. So for (a), all the good manufacturing practices, I think those are good. I do not believe -- I agree with the FDA, but I do not believe that the instrumentation is life-supporting or life-sustaining, you know, or of substantial importance in preventing impairment to human health. They are instruments. They do not stay in the patient. I also agree with the FDA, but I do not believe that the instrument presents a potential unreasonable risk in the appropriately trained surgeon. And then I believe sufficient information exists to establish special controls for urogynecologic surgical mesh, and I do agree with that. And that's the next question. Yeah.

DR. TALAMINI: So other Panel members?

Yeah, Dr. Hicks.

DR. HICKS: Dr. Iglesia, I mean, I think early on you really hit on the problem, the dilemma that we're in here, and there's a philosophical problem here, the way I perceive this. There's the instrument, there's the procedure, and there's the surgeon. So there's this triangle that's going on here. It would seem common sense to me that whatever the

instrument is, if it breaks, malfunctions, that's a problem that needs to be looked at. The problem is what if you -- and I think Dr. Efron hit on it here, about the blunt versus sharp trocars. The reality is you could take a hemostat, and you could do really bad damage with it. You know, it's doable.

So the question is -- what I worry about is that they make a product, somebody makes a product and it comes to you, and you do a thousand of these and you're so good at it. It's really a pretty dangerous instrument in the common surgeon's hand, but you write a paper about a thousand, and you can do it. And again, Jonathan talked about the fact that it's the credentialing responsibility and the training part of this. So trying to reduce this down with all of this philosophical stuff put together, are we just really responsible for -- we're not responsible for the training. We're not responsible for the utilization. That's somebody else's problem. The question is, where's that fine balance where they've done this instrument that you can do but nobody else can do? Dr. Iglesia is the only one at this table that has the technical skill, and she writes a thousand -- she writes a paper about a thousand times she's used it, but you and I, I mean, realistically we're just not technically adept to it. Does that fall in our hands, or is that again a credentialing problem?

DR. TALAMINI: So I wouldn't presume to answer for Dr. Fisher, but it seems to me the FDA feels very responsible regarding whether it's too sharp, too blunt, too angled, going to fall apart. But they also are very interested in being able to collect the data to know if a particular instrument, A, in the average trained surgeon's hands has a much worse record than instrument B in the average surgeon's hands, and absent this sort of

classification, it's very difficult for them to do that. That would be the way I would put it.

Dr. Fisher.

DR. FISHER: The thing that I would add that, you know, if you had this instrumentation just by itself, there's really not a whole lot you can do, okay? If you have the instrumentation with the mesh, then you can use the instrumentation to place the mesh. And like I have said before, we believe that the instrumentation is used, but really where we felt the clinical data was needed was in the proficiency of the clinician to be able to place the mesh the way that it was supposed to be placed. So, once again, you know, we're not discarding that.

You know, we have felt that if we were to look at training or require training, it would actually be with the placement of the mesh. But for the instrumentation itself, if someone were to tell us that we're changing the curvature by 10 degrees, well, we may not know -- or we're going to put a sharp tip on it, we may not know what that, how that could impact the device. Putting it in Class II will give us the ability to ask those questions, where currently we can't.

DR. TALAMINI: So looking at No. 3 in the set of questions that you have in front of you, you see what the FDA has proposed specifically for special controls for this as a Class II device, for these as a Class II device, including the potential labeling. So I would again ask whether you think those are appropriate, whether they're worded properly. Has anything been left out? Or, in general, do you think they are on target? And once we've sort of gone through these, we can go back and actually go through the questions officially.

Dr. Martens.

DR. MARTENS: Mark Martens.

First, I want to reiterate what Dr. Iglesia said. Urinary incontinence is a tremendous problem in the United States. You know, the amount of -- the number of women sitting in nursing homes using diapers is shameful. So I don't want to impact the use of these very, very effective and useful devices. I am concerned about the performance of these devices. Forget about, you know, the competence of the surgeon. I think that minor changes in the design, making it wider, the diameter bigger, to make it more durable is going to impact on what vessels and nerves that it hits. Making it thinner. To make it easier to miss the vessels, we'll make it possibly bend and then enter the bladder or another viscus.

So I think that -- so my only recommendation or my suggestion is I really think that the clinical performance needs to be done also. I'm the owner of several patents, none of which have impact here. But when I got into a laboratory and I have a device, I have a 110-pound resident that I have use the device, and they maybe can't put it in. And then I have 200-pound ex-football player resident that puts it and crushes the plastic components of the device. So I think that what's done in a cadaver and what's done in a lab with the average surgeon isn't representative of what happens in the real world.

Your comment about trocars is exactly like I felt. You think that a sharper trocar would cause more damage and therefore be a danger. Well, the amount of pressure you put with a sharper device, a non-reusable device and disposable device, makes it easier to get in and you have less perforation. So the impact of these devices and changing these

devices can only, I think, be measured with some clinical data.

Now, I don't want to impact the current use. I think they're already out there. There are millions of uses. I think it's easy for them to get the devices and say, just like you said, wow, there's 12 perforations, but that's with 1.2 million uses. It's obviously safe in the right hands.

DR. TALAMINI: So, Dr. Martens, Point 3 here says nonclinical performance testing must demonstrate that the device meets all design specifications, etc. Are you proposing that there be a special control related to clinical performance?

DR. MARTENS: Right, the collection of previous clinical data or, if it's a new device, new data. Clinical data.

DR. TALAMINI: Dr. Fisher, are there examples where special controls have been applied to Class II devices with respect to clinical data?

DR. FISHER: Yes, there have.

DR. TALAMINI: Do others have thoughts or comments on that?

Dr. Iglesia.

DR. IGLESIA: Well, as I said, I think that the vaginal mesh, transvaginal mesh used for prolapse is easier now because we have the registry and the 522 studies that are ongoing, which are going to easily satisfy the clinical data and the comparative data that we need. I think slings have already been proven, which is why -- and I will say that I was the only probably Panel member here who was also on the Panel in 2011. You know, they stayed as Class II. And so I think this information, including the -- you know, just this biocompatibility and the nonclinical stuff I think is pretty much all we need.

DR. TALAMINI: So you would not favor adding a special control regarding clinical data?

DR. IGLESIA: I don't think at this point for slings or colpopexy mesh, no. I think it's rather burdensome, actually.

DR. TALAMINI: Other thoughts? You know, we'll go around the table and address this directly when we answer the questions.

DR. IGLESIA: I will say one other thing, though. You know, I think what we need is more of the guidelines and know that societies are working on -- we have some guidelines with ACOG, and we've got the vice president of education here. And how we train people. I mean, Sandy has a lot of power in that, in how things are rolled out, but -- and the American Urogynecologic Society has put out guidelines on vaginal mesh. I'm not aware of any guidelines right now on sling stuff, but that's not to say that that can't be looked at in the future. And I really honestly feel like that that training component is going to be more important in mitigating some of these catastrophic injuries.

DR. TALAMINI: Dr. Faulx, on the phone, do you have thoughts or comments on what we've been discussing?

DR. FAULX: Hello, can you hear me? No, I don't really actually have anything else to add. It's been a good conversation.

DR. TALAMINI: Okay, thank you.

So before we directly go through this, these questions from the FDA, any other deliberations from the Panel? I feel like we've mostly covered the ground that these questions are going to cover, and I guess I would ask again, in terms of the specific

language of the special controls, the labeling, any other things that we've left out or that you think are on this list that shouldn't be?

(No response.)

DR. TALAMINI: No? Okay. So let's go ahead to the questions, then, and bring them up. And then I think after that, from a process point of view, we'll take a brief break before we move to the next issues.

DR. VALDES: My name is Thelma Valdes from FDA.

Panel Question No. 1. The FDA has identified the following risks to health of urogynecologic surgical mesh instrumentation based upon FDA's review of literature, information available to FDA regarding the marketed devices, and the Manufacturer and User facility Device Experience, or MAUDE, databases:

- Perioperative risks. Organ perforation or injury and bleeding (including hemorrhage and hematoma).
- Damage to blood vessels, nerves, connective tissue, and other structures. This may be caused by improperly designed and/or misused surgical mesh instrumentation. Clinical sequelae include pelvic pain and neuromuscular problems.
- Adverse Tissue Reaction. This may be caused by non-compatible materials.
- Infection. This may be due to inadequate sterilization and/or reprocessing instructions or procedures.

a. Please comment on whether this list completely and accurately identifies the risks to health presented by urogynecologic surgery mesh instrumentation.

b. And please comment on whether you disagree with inclusion of any of these risks, or whether you believe that any other risks should be included in the overall risk assessment when considering all indications for this device type.

DR. TALAMINI: Okay, thank you.

So, as yesterday, we'll start somewhere randomly at the table and go around in a circle and answer those questions.

Dr. Efron, could we start with you? And we'll go around to your right.

DR. EFRON: Jonathan Efron.

As to question 1a, I believe the list completely and accurately identifies the risks to health. And as to (b), I would -- I do not disagree that -- let me see. I do not think there are any other risks that should be included.

DR. TALAMINI: Okay, thanks.

Dr. Hicks.

DR. HICKS: My only concern is -- I mean, I agree with both, but under damage to blood vessels, nerves, connective tissue and all, it said this may be caused by improperly designed or misused instrumentation. The "and/or" there, I don't know how that works out. I mean, is that the -- we just talked about it. That's not part of the purview of this Committee. It's about training or, yeah, it's either the instrument can cause it, but we're not talking about misused instrumentation. I mean, that's a whole different area, isn't it?

DR. TALAMINI: Well, I think the "and/or" is a nod to the human device interface that we've been discussing.

DR. HICKS: Well, I'll ask Dr. Fisher. Is that a problem to leave that in or not?

DR. FISHER: No, I note what you said. Yeah, thank you.

DR. HICKS: Well, then, I mean, because what it means is that you can go back to anything in the operating room that's presently okay and take a Kelly clamp, and you misuse it and you going to get a problem, are you going to make that now a Class II? Every OR instrument we use, everything, pickups, everything is that now a Class II?

DR. TALAMINI: You know, again, in terms of this specific question, your point is a really good one. But, you know, when you look at these things with an angle and a bit of a swirl, it's pretty obvious they're not going be used for a lot of other things like a Kelly clamp will. So I can see that you're concerned about the drift there, but I think this is a unique enough situation. We've got your proviso in your answer, so --

DR. HICKS: Okay. But if a company -- if some companies that get affected by this have to spend a whole lot of money to go back, and it's appropriate that they do, then do I turn and say that I want you to get every other instrument that's used on a lap tray, I want it all to go through the same kind of thing and they need to do that?

DR. TALAMINI: Yeah.

DR. HICKS: Are we opening up that can of worms?

DR. FISHER: No. And we're also not getting into the practice of medicine. So if there's a device there, you know, I don't want misuse to be misconstrued that we're getting into the whole arena of practice of medicine.

DR. TALAMINI: Okay, great.

Dr. Afifi, (a) and (b).

DR. AFIFI: I'm not a clinician, but based on what I have learned from the material

provided and from the discussion, I think I would answer yes to both (a) and (b).

DR. TALAMINI: Thank you.

Dr. Carson.

DR. CARSON: I would also answer yes to (a) and (b).

DR. TALAMINI: Thanks.

Dr. Iglesia.

DR. IGLESIA: Cheryl Iglesia.

So, for (a), I agree with Dr. Hicks that the perioperative risk with organ perforation and vessel damage we can control by design of the instrument a little bit. But that user we can't. We probably won't have as much control, and I really do believe that most of the instruments that are out there for slings, and honestly for the vaginal mesh, right now they're probably okay. The only thing I would like to add for (b) is that issue of the attachment and the fragmentation, the release mechanism, and as it attaches with the sheath's covering and maybe incomplete, you know, device deployment or whatever, because I've seen that happen.

DR. TALAMINI: Okay, great.

Dr. Donatucci.

DR. DONATUCCI: I have nothing to add to that.

DR. TALAMINI: Thanks.

Dr. Fennal.

DR. FENNAL: Yes to (a) and (b).

DR. TALAMINI: Thank you.

And Dr. Martens.

DR. MARTENS: Just to support Dr. Iglesia, I also was going to mention that I think the fragmentation issue is something that is a risk. I was assuming you'd put it under the risk of the damage it would cause to blood vessels, nerves. But I think the retention even of any -- you know, any artificial product that doesn't cause damage initially may cause -- migrate and cause damage later. So I think it should be a risk.

DR. TALAMINI: Okay, good.

Dr. Faulx, on the phone, are you okay with (a) and (b)?

DR. FAULX: Yes, thank you.

DR. TALAMINI: Okay. So, Dr. Fisher, with the discussion points that you heard regarding more generally used instruments, the Panel agrees with a yes on both (a) and (b) for Question 1. Does that meet the FDA's needs?

DR. FISHER: Yes, thank you very much.

DR. TALAMINI: Okay, Question 2.

DR. VALDES: Panel Question 2: Section 513 of the Food, Drug, and Cosmetic Act states a device should be Class III if:

- insufficient information exists to determine that general controls are sufficient to provide reasonable assurance of its safety and effectiveness or that application of special controls would provide such assurance, and
- the device is life-supporting or life-sustaining, or for a use which is of substantial importance in preventing impairment of human health, or if the device presents a potential unreasonable risk of illness or injury.

A device should be Class II if:

- general controls are sufficient to provide reasonable assurance of the safety and effectiveness, and
- there is sufficient information to establish special controls to provide such assurance.

A device should be Class I if:

- general controls are sufficient to provide reasonable assurance of the safety and effectiveness, or
- insufficient information exists to:
    - determine that general controls are sufficient to provide reasonable assurance of the safety and effectiveness, or
    - establish special controls to provide such assurance, but
        i. is not purported or represented to be for a use in supporting or sustaining human life or for a use which is of substantial importance in preventing impairment of human health, and
        ii. does not present a potential unreasonable risk of illness or injury.

a. FDA believes that general controls alone are not sufficient to provide a reasonable assurance of safety and effectiveness for urogynecologic surgical mesh instrumentation. If you disagree, please discuss how general controls alone are sufficient to provide a reasonable assurance of safety and effectiveness for this device type. General controls may include:

i. Prohibition against adulterated or misbranded devices,

ii. Good Manufacturing Practices, or GMPs,

iii. Registration of manufacturing facilities,

iv. Listing of device types,

v. Record keeping.

b. FDA does not believe that urogynecologic surgical mesh instrumentation is "life-supporting or life-sustaining, or of substantial importance in preventing impairment of human health." Do you agree with this assessment? If not, please explain why.

c. FDA does not believe that urogynecologic surgical mesh instrumentation presents a "potential unreasonable risk of illness or injury." Do you agree with this assessment? If not, please explain why.

d. FDA believes sufficient information exists to establish special controls for urogynecologic surgical mesh instrumentation. Based on the information presented today, please discuss whether you believe that sufficient information exists to establish special controls that can provide a reasonable assurance of safety and effectiveness for this device type.

DR. TALAMINI: Thank you.

So, Panel, this is worded a little bit trickily. So, for (a), if you believe that special controls are needed for this device, you don't need to worry about all of the rest. So (a) is pretty straightforward from that point of view. So let me just ask each Panel member to go through (a), (b), (c), (d), and let us know how you feel.

Dr. Hicks, would you start for us? And we'll go the other direction this time, towards Dr. Efron.

DR. HICKS: I'm in compatibility with each of the FDA statements in (a), (b), (c), and (d).

DR. TALAMINI: Okay, thanks.

Dr. Efron.

DR. EFRON: I agree with each statement, (a), (b), (c), and (d).

DR. TALAMINI: Okay, thank you.

Dr. Martens.

DR. MARTENS: I also agree with each statement.

DR. TALAMINI: Thank you.

Dr. Fennal.

DR. FENNAL: I agree with all of their statements.

DR. TALAMINI: Thanks.

Dr. Donatucci.

DR. DONATUCCI: I agree.

DR. TALAMINI: Dr. Iglesia.

DR. IGLESIA: Agree.

DR. TALAMINI: Dr. Carson.

DR. CARSON: Agree.

DR. TALAMINI: Dr. Afifi.

DR. AFIFI: Agree.

DR. TALAMINI: And, Dr. Faulx, on the phone.

DR. FAULX: Agree. Thanks.

DR. TALAMINI: All right, terrific. So, Dr. Fisher, the Panel agrees unanimously with both (a), (b) -- all (a), (b), (c), and (d).

DR. FISHER: Thank very much.

DR. TALAMINI: Question 3.

DR. VALDES: Panel Question 3. FDA proposes the following special controls for urogynecologic surgical mesh instrumentation to provide reasonable assurance of their safety and effectiveness.

- The device must be demonstrated to be biocompatible;
- The device must be demonstrated to be sterile, including adequate reprocessing for reusable devices;
- Performance data must support the shelf life of the device by demonstrating package integrity and device functionality over the requested shelf life;
- Nonclinical performance testing must demonstrate that the device meets all design specifications and performance requirements, and that the device performs as intended under anticipated conditions of use; and
- Labeling must include:
    - Information regarding the mesh design that may be used with the device;
    - Detailed summary of the clinical evaluations pertinent to use of the

device;

- Expiration date; and
- Where components are intended to be sterilized by the user prior to initial use and/or are reusable, validated methods and instructions for sterilization and/or reprocessing of any reusable components.

Please discuss whether these special controls appropriately mitigate the identified risks to health of this device type, and whether you recommend additional or different special controls.

DR. TALAMINI: Thank you. So we've sort of gone through these in a fair discussion as well.

Dr. Iglesia, let me get you to start, and we'll go clockwise to your left.

DR. IGLESIA: Cheryl Iglesia.

I agree that these special controls are appropriate.

DR. TALAMINI: Okay. Dr. Carson.

DR. CARSON: Agree.

DR. TALAMINI: Dr. Afifi.

DR. AFIFI: Agree.

DR. TALAMINI: Dr. Hicks.

DR. HICKS: Agree.

DR. TALAMINI: Dr. Efron.

DR. EFRON: Agree.

DR. TALAMINI: Dr. Martens.

DR. MARTENS: I'm sorry. So, again, I agree in principle. I was told earlier that we're looking at the current devices on the market and not discussing what's going to be needed for future devices. So if that's the case -- and I'll defer to Dr. Iglesia because I think there's adequate clinical data out there to show that all of these devices are safe and effective and that the risks are well documented. If this sets the precedent for new devices, I will ask for clinical data on new devices.

DR. TALAMINI: Yeah. And you can certainly register your conviction that clinical information should be included as a special control. That's certainly okay.

DR. MARTENS: But this meeting is just for devices currently on the market.

DR. TALAMINI: Yeah.

DR. MARTENS: And I think that they're safe and have been adequately tested. So I agree with the statement.

DR. TALAMINI: Okay, great.

Dr. Fennal.

DR. FENNAL: Agree.

DR. TALAMINI: Dr. Donatucci.

DR. DONATUCCI: Agree.

DR. TALAMINI: Dr. Faulx. Dr. Faulx, are you there?

DR. FAULX: Agree.

DR. TALAMINI: Great.

DR. FAULX: Can you hear me?

DR. TALAMINI: Yeah, thank you.

So, Dr. Fisher, with the one proviso of Dr. Martens' potential call for clinical data as a special control, the Committee otherwise agrees with all of these statements.

DR. FISHER: Thank you, Dr. Talamini, and thanks to the Panel.

DR. TALAMINI: Great. So I think it might be appropriate to take a brief 10-minute break. I think checkout in the hotel is 11:00, but they're able to delay if you ask them at the front desk. So, again, I'll ask the Panel members not to discuss the issues during the break. It is now 10:09, so we'll plan to reconvene at 10:19.

Thank you very much.

(Off the record at 10:09 a.m.)

(On the record at 10:25 a.m.)

DR. TALAMINI: We have two very brief pieces of unfinished business. So I'll officially reconvene. The time now is 10:25. Two official pieces of business from the last session, and that is our Consumer Rep and our Industry Rep.

With respect to the last set of questions, Dr. Fennal, do you have any specific comments as our Consumer Representative?

DR. FENNAL: No additional comments at this time.

DR. TALAMINI: Thank you, Dr. Fennal.

Dr. Donatucci, as our Industry Representative?

DR. DONATUCCI: No additional comments.

DR. TALAMINI: Thank you.

Okay, we'll now move to the next two topics, thermal hemorrhoids device (LKX) and cushion hemorrhoid (LRL), since they are similar devices. I would like to invite the

FDA up to the podium to begin their presentation. The presenter is Dr. Mark Antonino.

Dr. Antonino.

MR. ANTONINO: Mister.

DR. TALAMINI: I'm sorry. Mister.

MR. ANTONINO: Good morning. My name is Mark Antonino. I am a biologist and premarket reviewer in FDA's Center for Devices and Radiological Health, commonly referred to as CDRH. Today I'll be presenting information regarding the effort to classify devices currently within two CDRH product codes which have not yet been categorized as Class I, II, or III. These devices are considered preamendments devices, as they were first marketed in the U.S. prior to the Medical Device Amendments of 1976.

A product code or procode is a unique three-letter code assigned by the FDA for each generic category of device, whether it has been formally classified by FDA or not. Each three-letter procode has an associated name. Procode names are generally created at the level of generic device group, which typically represents a set of devices having the same or similar intended use or common technology and which allows general product identification.

The product codes that are to be discussed today include, with their representative procode names:

- LKX – hemorrhoid heating and cooling devices, and
- LRL – hemorrhoid cushion devices.

For each procode we will be providing an introduction to the procode, a device description or representative device descriptions where several device types exist, an

indications for use statement or representative statements, the risks to health and mitigations that FDA has identified, and the classification FDA is proposing based on the risks and mitigations.

Following the presentation, FDA will be seeking the Panel's input on the identified risks and mitigation measures along with the proposed classifications.

The first procode in this category is LKX, hemorrhoid heating and cooling devices. The devices are designed to apply controlled cooling and conductive heating to hemorrhoids through the use of a probe that is partially inserted into the rectum. Since it is unclassified, there is no regulation associated with the product code. There have been 18 clearances for hemorrhoid heating and cooling devices (or modifications to previously cleared hemorrhoid heating and cooling devices) via the 510(k) process.

Please note: FDA is considering changing the name of the product code from device, thermal, hemorrhoids to heating and cooling hemorrhoid device to more accurately describe the types of devices under this product code. As you will see, the devices operate in similar ways and have similar indications for use statements.

Here are examples of the methods, as described by the manufacturers, used to deliver heating and cooling to hemorrhoids in the category known as LKX. They are representative of the devices found under this product code. For example, manufacturer device descriptions state the following:

- A device consisting of a module encased in plastic which houses a battery power source and control system. One cable terminates in an anal terminal or probe. Temperature range is adjustable from 37°C to 45°C.

- A device consisting of a hard plastic liquid container that is kept in the freezer until use.
- A sealed plastic device that has been anatomically designed to fit the shape of the anal canal; device contains coolant material.
- An anatomically designed sealed plastic bag, enclosed in a medical grade cloth outer wrapper for comfort.

This slide outlines examples of the indications for use statements. They are representative of the devices found under this product code and they include:

- The apparatus is intended to apply controlled, conductive heating to hemorrhoids.
- Intended to provide temporary relief of the symptoms of hemorrhoids through the application of mild heating.
- Treatment of external hemorrhoids by applying cold therapy (cryotherapy) directly to swollen hemorrhoidal veins.
- Relief of hemorrhoidal discomfort through direct application of controlled cold to affected tissues.

The second procode in this category is LRL, hemorrhoid cushions. Hemorrhoid cushion devices are designed to temporarily relieve the pain and pressure caused by hemorrhoids through use of an inflatable/non-inflatable cushion or a plastic seat. Since it is unclassified, there is no regulation associated with the product code. There have been three clearances for hemorrhoid cushions (or modifications to previously cleared hemorrhoid cushion devices) via the 510(k) process.

The device descriptions shown here are representative of these devices found under this product code. Example device descriptions are an inflatable/non-inflatable cushion or plastic seat and designed to temporarily relieve pain and pressure caused by hemorrhoids.

The indications for use statements shown here are representative of the devices found under this product code. They include:

- For the temporary relief from the pain and pressure of hemorrhoids. The device is for external use only.
- Intended for the home convalescent patient with perineal discomfort.

To determine the appropriate classification for hemorrhoid devices under product codes LRL and LKX, we identify the risks associated with these devices and possible mitigations for these risks. We will be asking for the Panel's input on the lists of risks and mitigations.

To identify the risks of these devices, we used FDA's MAUDE database which houses medical device reports, known as MDRs, submitted to the FDA by mandatory reporters such as manufacturers, importers, and device user facilities and voluntary reporters such as healthcare professionals, patients, and consumers. We also used FDA's Medical Device Recalls database, information available to FDA regarding cleared devices, general use search engines, and PubMed.

Searches of the MAUDE and Medical Device Recalls databases returned no result for both procodes LKX and LRL. Additional results were obtained from searches of 510(k)-cleared information available to FDA or general use search engines or PubMed using key

search terms. PubMed key search terms included hemorrhoid cushion, hemorrhoid heating and hemorrhoid cooling. And four applicable studies were identified from the search. The literature search did not provide evidence of any safety concerns regarding the use of heating or cooling to hemorrhoid devices and hemorrhoid cushions.

Based on the additional searches, risks to health have been parsed into three groups:

- Risks to health for heating and cooling hemorrhoid devices under product code LKX;
- Risks to health for electrically powered hemorrhoid devices that deliver heat under product code LKX; and
- Risks to health for hemorrhoid cushion devices under product code LRL.

For each of the identified risks, FDA is recommending specific mitigation measures, as shown on the following slides.

Based on the searches, we identified these risks to health for heating and cooling hemorrhoid devices under product code LKX and hemorrhoid cushion devices under product code LRL. Identified risks include device failure and tissue injury, operator error, adverse tissue reaction, and infection. FDA believes that special controls will not be required and that general controls are sufficient to provide a reasonable assurance of the safety and effectiveness of heating and cooling hemorrhoid devices and hemorrhoid cushion devices.

Class I controls include, as Marjorie described, registration and listing, good manufacturing practices, or GMPs, prohibition against adulteration and misbranding, and

labeling devices according to FDA regulations.

Class I general controls for heating and cooling hemorrhoid devices align with FDA's regulation of enema kits. Enema kits are devices intended to instill water or other fluids into the colon through a nozzle inserted into the rectum to promote evacuation of the contents of the lower colon. The device consists of a container for fluid connected to the nozzle either directly or via tubing. Enema kits and heating/cooling hemorrhoid devices under product code LKX have similar identified risks for device failure/tissue injury, operator error, adverse tissue reaction (biocompatibility), and therefore FDA proposes that general controls are sufficient to provide a reasonable assurance of the safety and effectiveness for heating and cooling hemorrhoid devices under product code LKX.

Based on the searches, we identified these risks to health for heating hemorrhoid devices that deliver electrically powered heat under product code LKX. Identified risks include electrical shock hazard, adverse tissue reaction, device failure/tissue injury, operator error, and infection. For many of the risks, there are standard test methods to which the mitigation measures refer. FDA recommends the following mitigation measures:

- The patient contacting materials of the device must be demonstrated to be biocompatible;
- Performance data must demonstrate that the device performs as intended under the anticipated conditions of use. Performance testing should include electrical safety and electromagnetic compatibility; and

- Adequate device labeling that includes a description of the device, instructions for use of the device, and proper cleaning and care of the device.

FDA is primarily concerned with the risk of electrical shock and change in the physicochemical characteristics of the polymer when heated at higher temperatures for a sustained duration as achieved in hemorrhoid devices that deliver electrically powered heat under product code LKX. We propose that these mitigations be implemented as special controls as part of the device regulation process and will be presented in further detail in the following slides.

Based on the information presented, FDA is proposing two classifications for hemorrhoid cooling and heating devices. For the first classification, heating and cooling hemorrhoid devices, we identify the devices as follows:

Cooling and heating hemorrhoid devices consist of a probe that is inserted partially into the rectum and use cooling or conductive heating to temporarily relieve pain and pressure caused by hemorrhoids. The probe may contain a liquid to deliver heat or cold therapy. The device may alternatively use an electrical element to deliver heat therapy.

Based on the risks and mitigations identified, we propose the following regulation for hemorrhoid cooling and heating devices:

1. Class II (special controls) for electrically powered hemorrhoid devices that deliver heat. The special controls for this device are:
    a. The patient-contacting materials of the device must be demonstrated to be biocompatible.

b. Performance data must demonstrate that the device performs as intended under anticipated conditions of use. At a minimum, the following performance characteristics must be tested:

   i. Performance bench testing must demonstrate that the device is durable for repeated use.

   ii. Performance testing must verify the maximum treatment temperature is not exceeded.

   iii. Performance testing must evaluate the mechanical integrity of the device, including the structural strength.

   iv. Appropriate analysis and nonclinical testing must be conducted to validate electrical safety and electromagnetic compatibility.

c. Labeling must include the following:

   i. A description of the device and operational parameters.

   ii. Detailed instructions for the user to properly clean, disinfect, and maintain the device over the intended use life.

   iii. A summary which describes the possible susceptibility to electrical hazards associated and to electromagnetic interference with the use of the device.

We propose the following general controls for hemorrhoid devices that contain a liquid to deliver heat or cold therapy:

2. Class I (general controls) for hemorrhoid devices that contain a liquid to

deliver heat or cold therapy. The device is exempt from the premarket notification procedures in Subpart E of Part 807 of this chapter subject to 876.9.

Based on the risks and mitigations identified, we propose the following regulation for hemorrhoid cushion devices. We identify the devices as follows:

A hemorrhoid cushion is an inflatable/non-inflatable pillow or plastic seat used to temporarily relieve pain and pressure caused by hemorrhoids.

Based on the information presented, FDA is proposing the following classification:

Class I (general controls). The device is exempt from premarket notification procedures in Subpart E of Part 807 of this chapter subject to 876.9.

In your discussion today, we will ask you questions about the risks FDA has identified, the proposed mitigations, and the proposed classifications as Class I and II.

This is the end of my presentation. At this point, I would like to ask if there are any clarifying questions from the panelists regarding the presentation.

DR. TALAMINI: Thank you very much.

So, Panel, you see the framework that the FDA is proposing for these devices that predated the classification system. Clarification questions on that framework?

Dr. Hicks.

DR. HICKS: Yes, a question for you, Dr. Fisher. Knowing that it would be considered a Class I with just general controls, where does it fall again? And I think you explained this earlier, unless I missed it, about the claims that they make about the product. Is that cleared by -- who's that cleared by so they can label something and put it

out there?

DR. TALAMINI: Do you mean marketing claims?

DR. HICKS: Yeah. In other words, they say there's temporary relief of pain caused by hemorrhoids. Does the product actually do that? You know, is that the efficacy?

DR. FISHER: The efficacy for this, is that what you're saying?

DR. HICKS: Right.

DR. FISHER: So there are a variety of things that we would look at. You know, one, we would look at the medical claim. In this situation for the treatment of hemorrhoids, if it was an inflatable cushion or if it was one of these kind of suppository devices that is inserted with no electrical component, we feel pretty confident that if they didn't -- if they kept the claim to treatment of hemorrhoids, that we would be fine with that. The only exception that we're suggesting here is if these are electrically controlled --

DR. HICKS: Right.

DR. FISHER: -- that we would be -- the same thing.

DR. HICKS: I think early this morning you did the prep for us on this. There is somewhere that somebody looks at the claim.

DR. FISHER: Marjorie, do you want to address this? It's a question about intended use or just the labeling claims.

DR. HICKS: In other words, they make the claims -- I gave the example. I think it was something with food supplements. That falls into another -- who does that fall under? If they make claims about food supplements, it doesn't come here. It comes to some other committee or --

MS. SHULMAN: Yes, this is Marjorie Shulman.

What we're talking about if it's a medical device indication or claim, we'll review it as a medical device. If it doesn't have a medical claim such as -- supplements aren't regulated by the Center for Devices. They're regulated by another entity.

DR. HICKS: You're saying relief -- temporary relief of pain is what it says. Do they have to justify that? Does anybody look at that to see if there's any study ever to say that it does anything?

MS. SHULMAN: Well, that would be an indication, and that's what we would look at in the 510(k). Or if it went into Class I, we believe that the general controls can handle it.

DR. HICKS: Okay.

DR. TALAMINI: Dr. Martens.

DR. MARTENS: Thank you, Mr. Antonino, a very clear presentation. My question to you is, is there a reason why you used the specific wording, "electrically powered heating devices," because that's the only one on the market? The reason I bring this up is 21 years ago my first interaction with this Committee was based on the uterine ablation devices, which the first one was an electrically powered heating device called the Thermachoice. Within 2 years after that, they developed an electrically powered cryo device. So your current terminology wouldn't apply to that, correct?

MR. ANTONINO: No. We're aware of only heating devices at this point for treatment of hemorrhoids.

DR. TALAMINI: Other clarification questions?

Dr. Carson.

(Off microphone response.)

DR. TALAMINI: No? Okay, thank you very much for your clear presentation.

So just like earlier this morning, it's now our opportunity to deliberate amongst ourselves with respect to this framework and then directly answer the questions that will be -- that are in here put forth by the FDA. So I guess I would ask the Panel, generally, does anybody disagree with the framework that you've seen in terms of these devices falling into mostly Class I with one -- the one that plugs in being Class II? Are there issues or discussion points that the Panel wants to bring forward with regard to the overall framework? Nothing?

Dr. Faulx, on the phone, any issues with the framework?

DR. FAULX: No, I have no issues.

DR. TALAMINI: How about specifically with the list of -- you know, if you look at the questions again in front of you, for Question No. 1 -- these are actually pretty long questions, but in terms of the lists that you see there for risks, is there anything that you feel has been left out or are on those lists inappropriately?

DR. IGLESIA: I have a comment.

DR. TALAMINI: Dr. Iglesia.

DR. IGLESIA: Cheryl Iglesia.

I just have a comment. So if these are specifically for hemorrhoids, but then -- and the indication is for hemorrhoids, but then somebody uses it, say, for a woman who has hemorrhoids but also had an episiotomy, you know, and they're using this to say this is

also for perineal -- you know, a cushion for perineal issues, I mean, she does have a hemorrhoid, but it's kind of being marketed for that kind of indication. We don't really regulate that practice, what people end up doing, but I could see this happening, is what I'm trying to say, because it's a quite common condition, peripartum.

DR. TALAMINI: Sure. Dr. Fisher.

DR. FISHER: Okay, so two things here. You're right. You know, we would -- you know, a device would be cleared for a specific indication, and then once it gets out there, if it's used for something else, that would be considered practice of medicine. But one of the general controls -- this goes back to what Dr. Hicks was asking I think earlier. Going back to the general controls, labeling is a general control, and labeling has to be truthful and not misleading. So if there was an approved device out there and it was being marketed outside that indication, then that would become a compliance issue, and we would allow compliance to take action if they felt that it was being misrepresented or the information was misleading.

DR. TALAMINI: Dr. Martens.

DR. MARTENS: So we're allowed to discuss labeling? Because Dr. Iglesia's comments -- the only thing I was going to bring up is that hemorrhoids, during the delivery process, is a very common occurrence, and I'd hate to see this used and marketed as something to take care of hemorrhoids at the time of delivery or immediately after. I'd like to have a cooling-down period, so to say.

DR. FISHER: So to speak?

DR. MARTENS: So to speak, to maybe, you know, 4 to 6 weeks.

DR. TALAMINI: I don't know whether any of that exists in the current labeling. I don't think so. So that's an excellent comment.

I think, without additional comments and with the sense that the Panel agrees with this general framework, we can probably move directly to the questions. Is everybody okay with that? Is the Panel okay with that?

Okay. So, FDA, let's go ahead with the specific questions. You will have to focus because the questions are long.

DR. MARIANI: Good morning. So we are going to be going through our Panel questions.

Panel Question No. 1, the first question to the Panel involves identified risks: FDA has identified the following risks to health for hemorrhoid cushion devices under product code LRL:

- Device failure or tissue injury
- Operator error, and
- Adverse tissue reaction

Please comment on whether you agree with inclusion of all of the risks in the overall risk assessment of hemorrhoid cushion devices under product code LRL.

In addition, please comment on whether you believe that any additional risks should be included in the overall risk assessment of these hemorrhoid devices.

DR. TALAMINI: Thank you.

So I would -- in your Panel packet, and maybe this is the second -- at least in mine it's the second set and not the first set. So the LRL is second and LKX is first in your -- so

you have to go to the second set for this. So we'll just go around the Panel.

Dr. Martens, for Question 1, do you agree that the list is correct, and would you add any additional risks?

DR. MARTENS: I agree, the list is correct and wouldn't add anything.

DR. TALAMINI: Thank you.

Dr. Efron.

DR. EFRON: Agree.

DR. TALAMINI: Dr. Hicks.

DR. HICKS: Agree.

DR. TALAMINI: Dr. Afifi.

DR. AFIFI: Agree.

DR. TALAMINI: Dr. Carson.

DR. CARSON: Agree.

DR. TALAMINI: Dr. Iglesia.

DR. IGLESIA: Agree.

DR. TALAMINI: Dr. Donatucci.

DR. DONATUCCI: Agree.

DR. TALAMINI: Dr. Fennal.

DR. FENNAL: Agree.

DR. TALAMINI: Dr. Faulx.

DR. FAULX: Agree.

DR. TALAMINI: Okay. So with respect to Question 1, Dr. Fisher, the Panel agrees.

DR. FISHER: Thank you.

DR. TALAMINI: Question 2.

DR. MARIANI: FDA's second question to the Panel relates to the classification.

Section 513 of the Food, Drug, and Cosmetic Act states a device should be Class III if:

- insufficient information exists to determine that general controls are sufficient to provide reasonable assurance of its safety and effectiveness, or that application of special controls would provide such assurance, and
- the device is life-supporting or life-sustaining, or for a use which is of substantial importance in preventing impairment of human health, or if the device presents a potential unreasonable risk of illness or injury.

A device should be Class II if:

- general controls by themselves are insufficient to provide reasonable assurance of the safety and effectiveness, and
- there is sufficient information to establish special controls to provide such assurance.

A device should be Class I if:

- general controls are sufficient to provide reasonable assurance of the safety and effectiveness, or
- insufficient information exists to:
    - determine that general controls are sufficient to provide reasonable assurance of the safety and effectiveness, or

- establish special controls to provide such assurance, but
    i. is not purported or represented to be for a use in supporting or sustaining human life or for a use which is of substantial importance in preventing impairment of human health, and
    ii. does not present a potential unreasonable risk of illness or injury.

FDA does not believe that special controls will be required for hemorrhoid cushion devices under product code LRL and that general controls will be sufficient to provide a reasonable assurance of the safety and effectiveness for hemorrhoid cushion devices. As such, FDA believes that Class I is the appropriate classification for hemorrhoid cushion devices under product code LRL.

Please discuss whether you agree with FDA's proposed classification of Class I with general controls for hemorrhoid cushion devices under product code LRL. If you do not agree with FDA's proposed classification, please provide your rationale for recommending a different classification.

DR. TALAMINI: Thank you.

So let's start with Dr. Carson, and then we'll go around to the right. Do you agree with Class I and general controls?

DR. CARSON: I agree, low risk.

DR. TALAMINI: Dr. Iglesia.

DR. IGLESIA: Agree.

DR. TALAMINI: Dr. Donatucci.

DR. DONATUCCI: Agree.

DR. TALAMINI: Dr. Fennal.

DR. FENNAL: Agree.

DR. TALAMINI: Dr. Martens.

DR. MARTENS: Agree.

DR. TALAMINI: Dr. Efron.

DR. EFRON: Agree.

DR. TALAMINI: Dr. Hicks.

DR. HICKS: Agree.

DR. TALAMINI: Dr. Faulx.

DR. FAULX: Agree.

DR. TALAMINI: So --

DR. AFIFI: Afifi.

DR. TALAMINI: Oh, I'm sorry, Dr. Afifi.

DR. AFIFI: Agree.

DR. TALAMINI: Thank you.

So, Dr. Fisher, with respect to this question, the Panel indeed agrees Class I with general controls.

DR. FISHER: Thank you.

DR. MARIANI: So now we're on to our classification of hemorrhoid devices, LKX. Sorry about the confusion earlier.

Please discuss whether you agree -- oh, it skipped to Slide 6. Sorry. My apologies.

The first question to the Panel involves identified risks. This is going to be in the front, the first page.

DR. TALAMINI: So this is now two pages back. It says, at the top, Classification of Hemorrhoid Devices, LKX, at the top of the page.

DR. MARIANI: All right. The first question to the Panel involves identified risks. FDA has identified the following risks to human health for heating and cooling hemorrhoid devices and electrically powered hemorrhoid devices that deliver heat under product code LKX.

For heating and cooling hemorrhoid devices, risks include:

- Device failure or tissue injury
- Operator error
- Adverse tissue reaction, and
- Infection

For electrically powered hemorrhoid devices that deliver heat, the identified risks are:

- Electrical shock hazard
- Adverse tissue reaction
- Device failure or tissue injury
- Operator error, and
- Infection

Please comment on whether you agree with the inclusion of all of the risks in the overall risk assessment of heating and cooling of hemorrhoid devices (including

electrically powered hemorrhoid devices that will deliver heat) under product code LKX.

In addition, please comment on whether you believe that any additional risks should be included in the overall risk assessment of these hemorrhoid devices.

DR. TALAMINI: Thank you.

Dr. Hicks, the risk lists, agree? And we'll move to your left from there. Question 1.

DR. HICKS: I guess under tissue injury in general, that would be trauma, is what I'm thinking about. So that would be included under device failure/tissue injury?

DR. TALAMINI: It might be operator error. The operator is the patient in this case.

DR. HICKS: Right. I just think that it needs to be clarified that there could be traumatic injury.

DR. TALAMINI: Okay, fair enough.

Dr. Efron.

DR. EFRON: Agree.

DR. TALAMINI: Dr. Martens.

DR. MARTENS: Agree.

DR. TALAMINI: Would both of you want to see potential trauma on that list, tissue injury due to trauma?

DR. EFRON: Well, I think in my opinion it's sort of implied, but tissue injury is a result from trauma, heat, I mean, everything that goes underneath that.

DR. MARTENS: I agree. And it's incorporated under tissue injury for me.

DR. TALAMINI: Okay. Dr. Fennal.

DR. FENNAL: Agree.

DR. TALAMINI: Dr. Donatucci.

DR. DONATUCCI: Agree.

DR. TALAMINI: Dr. Iglesia.

DR. IGLESIA: Agree and no additions.

DR. TALAMINI: Dr. Carson.

DR. CARSON: Agree and no additions.

DR. TALAMINI: Dr. Afifi.

DR. AFIFI: Agree.

DR. TALAMINI: Dr. Faulx.

DR. FAULX: Agree.

DR. TALAMINI: Okay. Dr. Fisher, the Panel agrees in general with the lists, with potential additional thinking about traumatic injury from insertion.

DR. FISHER: Right, I've noted Dr. Hicks' comment. Thank you.

DR. TALAMINI: Thanks. Question 2.

DR. MARIANI: FDA's second question to the Panel relates to the classification.

Section 513 of the Food, Drug, and Cosmetic Act states a device should be Class III if:

- insufficient information exists to determine that general controls are sufficient to provide reasonable assurance of its safety and effectiveness, or that application of special controls would provide such assurance, and
- the device is life-supporting or life-sustaining, or for a use which is of substantial importance in preventing impairment of human health, or if the

device presents a potential unreasonable risk of illness or injury.

A device should be Class II if:

- general controls by themselves are insufficient to provide reasonable assurance of the safety and effectiveness, and
- there is sufficient information to establish special controls to provide such assurance.

A device should be Class I if:

- general controls are sufficient to provide reasonable assurance of the safety and effectiveness, or
- insufficient information exists to:
    - determine that general controls are sufficient to provide reasonable assurance of the safety and effectiveness, or
    - establish special controls to provide such assurance, but
        i. is not purported or represented to be for a use in supporting or sustaining human life or for a use which is of substantial importance in preventing impairment of human health, and
        ii. does not present a potential unreasonable risk of illness or injury.

FDA does not believe that special controls will be required for hemorrhoid devices that contain a liquid to deliver heat or cold therapy under product code LKX and that general controls will be sufficient to provide a reasonable assurance of the safety and effectiveness for hemorrhoid devices that contain a liquid to deliver heat or cold therapy.

As such, FDA believes that Class I is the appropriate classification for hemorrhoid devices that contain a liquid to deliver heat or cold therapy under product code LKX.

Please discuss whether you agree with FDA's proposed classification of Class I with general controls for hemorrhoid devices that contain a liquid to deliver heat or cold therapy under product code LKX. If you do not agree with FDA's proposed classification, please provide your rationale for recommending a different classification.

DR. TALAMINI: So why don't we do Question 2a separately.

Dr. Iglesia.

DR. IGLESIA: I agree, Class I.

DR. TALAMINI: Okay. Dr. Carson.

DR. CARSON: I agree, Class I.

DR. TALAMINI: Dr. Afifi.

DR. AFIFI: I agree.

DR. TALAMINI: Dr. Hicks.

(Off microphone response.)

DR. TALAMINI: Okay. Dr. Efron.

DR. EFRON: Agree.

DR. TALAMINI: Dr. Martens.

DR. MARTENS: I agree, Class I.

DR. TALAMINI: Dr. Fennal.

DR. FENNAL: Agree.

DR. TALAMINI: Dr. Donatucci.

DR. DONATUCCI: Agree.

DR. TALAMINI: Dr. Hicks, back to you.

DR. HICKS: My only question is about -- and I gather, would it be -- if it's a I, would it be evaluated for the liquid that's inside? In other words, if the liquid were to leak or something like that, if it contains a liquid to deliver heat or cold, if there's some kind of, you know, coolant or whatever is inside there, if that leaks out, is that an issue?

DR. FISHER: So we would be asking for a list of the components, but there would not be testing that we would require on the liquid. So it's a requirement that you'd list everything that's in there.

DR. HICKS: Okay.

DR. TALAMINI: As a Class I.

DR. FISHER: As a Class I.

DR. HICKS: As an example, in kids' lunchboxes, the coolant they put in the freezer.

DR. FISHER: Right, right, right.

DR. HICKS: I don't know what's inside that, and hopefully you'll look to make sure it's safe.

DR. FISHER: No, that's consumer products, but that's okay.

DR. TALAMINI: So your vote, Dr. Hicks?

DR. HICKS: Yes.

DR. TALAMINI: Okay. So, Dr. Fisher -- did I miss anybody? Oh, Dr. Faulx.

DR. FAULX: Yes. Thanks.

DR. TALAMINI: Yes, okay. So, Dr. Fisher, the Panel agrees with the classification of

Class I for these devices in Question 2a.

So 2b.

DR. FISHER: Thank you.

DR. MARIANI: FDA believes general controls by themselves are insufficient to provide reasonable assurance of the safety and effectiveness, and sufficient information exists to establish special controls to adequately mitigate the risks to health and provide reasonable assurance of device safety and effectiveness for electrically powered hemorrhoid devices that deliver heat under product code LKX. As such, FDA believes that Class II is the appropriate classification for electrically powered hemorrhoid devices that deliver heat under product code LKX.

Following is a risk/mitigation table, which outlines the identified risks to health for this device type and the recommended controls to mitigate the identified risks.

For a risk of electrical shock, the recommended mitigation measures include performance testing and labeling.

For a risk of adverse tissue reaction, the recommended mitigation measures include biocompatibility and labeling.

For a risk of device failure or tissue injury, recommended mitigation measures include performance testing and labeling.

For a risk of operator error, recommended mitigation measures include labeling.

For a risk of infection, the recommended mitigation measures include labeling.

Please discuss whether the following special controls appropriately mitigate the identified risks to health for electrically powered hemorrhoid devices that deliver heat

under product code LKX and whether additional or different special controls are recommended.

i. The patient-contacting components of the device must be demonstrated to be biocompatible.

ii. Performance data must demonstrate that the device performs as intended under anticipated conditions of use. At a minimum, the following performance characteristics must be tested:

- Performance bench testing must demonstrate that the device is durable for repeated use.
- Performance testing must verify that the maximum treatment temperature is not exceeded.
- Performance testing must evaluate the mechanical integrity of the device, including the structural strength.
- Appropriate analysis and nonclinical testing must be conducted to validate electrical safety and electromagnetic compatibility.

iii. The labeling must include the following:

- A description of the device and operational parameters.
- Detailed instructions for the user to properly clean, disinfect, and maintain the device over the intended use life.
- A summary which describes the possible susceptibility to electrical hazards associated, and to electromagnetic interference with the use of the device.

Please discuss whether you agree with FDA's proposed classification of Class II with special controls for electrically powered hemorrhoid devices that deliver heat under product code LKX. If you do not agree with FDA's proposed classification, please provide your rationale for recommending a different classification.

DR. TALAMINI: Okay, Panel members. Dr. Martens, would you like to begin? And we'll go clockwise. Do you agree with Class II with special controls as delineated in this question?

DR. MARTENS: I agree.

DR. TALAMINI: Dr. Fennal.

DR. FENNAL: Agree.

DR. TALAMINI: Dr. Donatucci.

DR. DONATUCCI: Agree.

DR. TALAMINI: Dr. Iglesia.

DR. IGLESIA: Agree.

DR. TALAMINI: Dr. Carson.

DR. CARSON: I agree.

DR. TALAMINI: Dr. Afifi.

DR. AFIFI: Agree.

DR. TALAMINI: Dr. Hicks.

DR. HICKS: Agree.

DR. TALAMINI: Dr. Efron.

DR. EFRON: I agree.

DR. TALAMINI: Dr. Faulx.

DR. FAULX: I agree.

DR. TALAMINI: Dr. Fisher, we have a unanimous Panel endorsement of Class II with this specific list of special controls.

DR. FISHER: Thank you. It's an exciting class of devices.

(Laughter.)

DR. TALAMINI: Okay. Once again, we need to hear directly from our Consumer Representative and Industry Representative.

Dr. Fennal, do you have additional comments with regard to these two devices?

DR. FENNAL: No additional comment.

DR. TALAMINI: And, Dr. Donatucci, as our Industry Rep?

DR. DONATUCCI: Nothing further.

DR. TALAMINI: Okay. Okay, we have -- our final topic for the day is the FDA -- the separator, automated blood cell and plasma therapeutic (LKN) device. And we'd like to invite the FDA up to the podium to begin their presentation on this next topic, and I think this is Dr. Angela Mariani. For this topic we have an additional Panel member, Dr. Louis DePalma.

Dr. DePalma, would you like to introduce yourself?

DR. DePALMA: Yes, thank you. I am Division Director of Clinical Pathology at the George Washington University Hospital, and I am Professor of Pathology and of Anatomy and Regenerative Biology at the GW School of Medicine.

DR. TALAMINI: Thank you.

Dr. Mariani.

DR. MARIANI: Great. Good morning, panelists. My name is Angela Mariani, and I will be presenting on behalf of the Renal Devices Branch for the classification of centrifuge systems for therapeutic blood cell and plasma separation.

As discussed earlier by 510(k) Staff and Mark in the previous presentation, this is a classification, not a reclassification panel meeting.

Centrifuge-type therapeutic apheresis devices are designed to separate plasma or blood components from whole blood. These devices are regulated under the product code LKN. Since it is unclassified, there is no regulation associated with this product code. Under this product code, there have been 17 clearances for centrifuge-type therapeutic apheresis devices and two clearances for accessories.

These devices were all found substantially equivalent to preamendment devices and cleared through the 510(k) process between 1983 and 2015. It should be noted that this product code is designated for use by the Center for Devices and Radiological Health for the therapeutic use of centrifuge-type apheresis equipment. Similar equipment is used for blood banking, but these devices are regulated by the Center for Biologics Evaluation and Research. This product code also does not apply to membrane-type apheresis devices.

Centrifuge-type therapeutic apheresis devices are designed to separate plasma or blood components from whole blood. These devices are typically automated continuous-flow systems that are comprised of a blood component separator instrument that uses pumps, valves, and sensors as well as a disposable apheresis kit, including an

extracorporeal circuit specific to the procedure being performed.

The blood component separator draws whole blood from a patient, separates the blood into its components, utilizing centrifugal force as the basis of operation, collects one or more of the blood components, and returns the remainder of the blood components to the patient.

This diagram depicts the general concept. Blood is drawn into the device from the patient and is separated into its components through centrifugal force. This spinning causes a separation of the blood components based on the density of each component. The distinct layers which form allow for the removal of specific cellular components or plasma prior to the return of the blood to the patient.

On this slide are shown examples of the indications for use statements. They are representative of the devices cleared under this product code. They include:

- May be used to perform therapeutic plasma exchange or plasma treatment.
- To remove plasma components and/or fluid.
- May be used to perform red blood cell exchange procedures for the transfusion management of sickle cell disease in adults and children.

Indications for use have also included the following, more general indications:

- For use in apheresis procedures involving donors and patients.
- To harvest cellular components from the blood of certain patients where the attending physician feels the removal of such components may benefit the patient.

To determine the appropriate classification for centrifuge-type therapeutic

apheresis devices, we sought to identify the risks associated with these devices. We will be asking for the Panel's input as to whether the list of risks is complete.

To identify the risks of these devices, we used FDA's MAUDE database and the information available to FDA regarding cleared devices. We also conducted a literature review on PubMed using representative key terms. Due to the volume of reports in the MAUDE system, the overall search was restricted to 5 years with individual review of the most recent 12 months of reports, except for deaths and injuries, which were reviewed for the entire 5-year period. To ensure we captured all risks, we also conducted a recall search for the same time period.

The MAUDE database was fully implemented in August 1996 and houses medical device reports (MDRs) submitted to the FDA by mandatory reporters such as manufacturers, importers, and device user facilities, and voluntary reporters such as health care professionals, patients, and consumers.

Searches of the MAUDE database returned 1,447 medical device records on centrifuge-type therapeutic apheresis devices from September 1st, 2010 to August 31st, 2015. These will be reviewed on the next slide.

Of note, several of the MDRs were reported for blood donation procedures, including mononuclear cell collection, which are outside the scope of this classification as these device functions are regulated by the FDA's Center for Biologics Evaluation and Research. The numbers were included, however, for the sake of completeness.

There were eight recalls for three different devices. These included corrections for issues related to air detection, excess loss of platelets, usability, and labeling. One recall

was a little more significant and involved the removal of a disposable set because of greater than anticipated red blood cell removal and anemia.

The reported adverse events fall into the following categories as defined by the person entering the report:

- Death
- Injury
- Malfunction, and
- No category assigned

The total MDRs vary during this period without clear trends.

There were a total of 21 deaths reported over this time period. Of note, one of the deaths in the most recent year was a nonhuman primate, so there was a total of 20 human deaths over this time period. We did an additional search of the death reports for the past 10 years, and this frequency appears to be relatively constant over time.

Many of the patients were critically ill and receiving urgent and emergent plasma exchange therapy. For this reason, the reported deaths were attributed to the patients' underlying condition and not the device.

Injury reports have been relatively unchanged except for the September 2010 to August 2011 reporting range, which is largely due to changes in company MDR evaluation processes, as noted. While these were labeled as injuries, they were not different from other MDRs in the "Malfunction" or "Other" categories.

Additionally, it should be noted that miscategorization in MDR reporting is common, and occasionally there are multiple MDRs for a single event, and similarly a

single event -- a single MDR can include multiple adverse events. Individual review of MDRs informed the categories of the risks that you will see on a later slide.

A literature review was conducted using the PubMed database. Representative search terms were used to identify relevant articles published between January of 1980 and September of 2014. FDA identified 32 articles that included relevant information on centrifuge devices marketed in the United States. The articles included clinical studies conducted in humans which specifically evaluated the safety and effectiveness of centrifuge devices used for therapeutic apheresis procedures, regardless of the indication.

After review of these articles, FDA believes that the adverse events for this device type are well described. The most frequent events were hypotension, symptomatic hypocalcemia, and allergic reactions. The events were typically non-serious and resolved without clinical consequences. The events were also consistent with those identified in the MDR search and were used to inform the risks to health listed on the next slide.

Here, are the categories of risks identified after review of the individual MDR reports, recalls, the review of the published literature, as well as FDA's review experience. We believe that this is a complete list of the risks to health for the devices under this product code. The Panel will be asked if this list is complete.

We believe all of these risks can be mitigated through the implementation of special controls. The Panel will be asked whether or not they believe that the proposed special controls are adequate to mitigate these risks. I will be discussing the specific mitigation measures as shown on the following slides.

The following table outlines the risk categories, examples of risks within the

category, and the recommended mitigation measures. Additional details regarding the mitigation measures are provided in later slides, which describe the proposed special controls.

For the risk of thrombosis in patient and the device, which could include clotting of the patient's vascular access or clotting in the extracorporeal circuit, the recommended mitigation measures are performance testing, sterility, labeling, and clinical performance testing.

For the identified risk of adverse tissue reaction, which could include allergic or hypersensitivity reactions, the recommended mitigation measures are biocompatibility, sterility, expiration date testing, and labeling.

For the risk of infection and pyrogen reactions, the mitigation measures are performance testing, sterility, expiration date testing, and labeling.

For the risk of failure of the device or disposables, the recommended mitigation measures are performance testing, expiration date testing, and labeling.

For air embolism, which can occur when the air enters the circuit and subsequently the patient's bloodstream, the recommended mitigation measures are performance testing and labeling.

For the identified risk of hemolysis, the mitigation measures are performance testing and labeling.

For the identified risk of blood loss or anemia, the mitigation measures are performance testing and labeling.

For toxic reaction to the anticoagulant, such as citrate toxicity, the mitigation

measures are performance testing, labeling, and clinical performance testing.

For the risk of electrical shock, the recommended mitigation measures are performance testing and labeling.

For the risk of fluid imbalance, which can result in fluid overload or hypovolemia, the recommended mitigation measures are performance testing, labeling, and clinical performance testing.

For inadequate separation of blood components, such as the unintended or excess removal of blood components, the mitigation measures are performance testing and clinical performance testing.

For operator error, such as the incorrect use of the device, the mitigation measures are usability performance testing and labeling.

We propose that these mitigations can be implemented as special controls as part of the device regulation process.

Based on the information we have available to us today, we are proposing the following regulatory classification. We identify the device as follows:

Centrifuge-type therapeutic apheresis device is an automated blood cell and plasma separator intended for the therapeutic separation of blood components from whole blood using centrifugal separation principles for the purpose of depletion or exchange of cellular blood components or plasma in the treatment of various illnesses. During treatment, blood is withdrawn from the patient and circulated through an extracorporeal circuit and centrifuge chamber, enabling the removal of cellular blood components or plasma based on the density of these substances.

The centrifuge-type therapeutic apheresis device is an automated intermittent-flow or continuous-flow system that consists of the following devices:

1. The automated blood cell and plasma separator instrument consists of pumps, valves, and sensors. It controls and monitors the parameters related to blood component processing, including the rate at which whole blood is pumped through the system, and the rate at which cellular blood components or plasma are removed from the patient. The automated blood cell and plasma separator draws whole blood from the patient, separates the blood into its components, utilizing centrifugal force as the basis of operation, removes one or more of the blood components, and returns the remainder of the blood components to the patient.
2. The therapeutic automated blood cell and plasma separator accessories include, but are not limited to, the disposable apheresis kit, plasma discard bags, tubing lines, and various treatment-related monitors, including pH, blood pressure, hematocrit, and blood recirculation monitors.

For the classification of this device we are proposing Class II. We believe the risks associated with these devices can be mitigated through the implementation of special controls. We will be asking for the Panel's input as to whether the proposed special controls adequately mitigate the associated risks, so please feel free to jot down any notes as I present the following special controls.

The special controls we propose for this device are:

1. The patient-contacting components of the device must be demonstrated to

be biocompatible.

2. Performance data must demonstrate that the device performs as intended under anticipated conditions of use, as follows:

    i. Functional testing must demonstrate:

        a. mechanical integrity of the device and disposables;

        b. device functionality in terms of separation and removal of blood components;

        c. device functionality in terms of fluid and anticoagulation management when the device is used according to its labeling;

        d. proper functionality of device safeguards and alarms.

Performance data must demonstrate that the device performs as intended, including:

ii. Mechanical hemolysis testing must be conducted;

iii. A system-level hazard analysis that confirms that the device does not perform in an unexpected and/or unsafe manner;

iv. Software verification and validation testing must be performed;

v. Appropriate analysis and nonclinical testing must be conducted to validate electrical safety;

vi. Appropriate analysis and nonclinical testing must be conducted to validate electromagnetic compatibility;

vii. Performance data must demonstrate sterility of the device; and

viii. Performance data must support the shelf life of the device for continued sterility, package integrity, and functionality over the requested shelf life.

3. Labeling must include the following:

i. A description of the device and individual components, accessories that need to be used with the system, operational parameters, and software version;

ii. A description of the pretreatment performance and post-treatment steps needed to safely perform each therapy mode (if more than one may be performed);

iii. A description of the alarms included in the system, the alarm format (for example, visual or audio), the suspected cause of the alarm condition, and how the user must respond to the alarm;

iv. Detailed instructions for the user to properly clean, disinfect, and maintain the device.

Labeling must also include:

v. A detailed summary of the device-related and procedure-related complications pertinent to the use of the device;

vi. A summary which describes the possible susceptibility to electromagnetic interference and possible electrical hazards associated with the use of the device; and

vii. A troubleshooting guide for users to reference if problems are

encountered.

4. Clinical performance testing must demonstrate that the device performs as intended under anticipated conditions of use and document any adverse events observed during clinical use.

This is the end of my scheduled presentation, and at this point I would like to ask if there are any clarifying questions from the panelists regarding our presentation.

DR. TALAMINI: Thank you. Obviously, this is not the hemorrhoid cushion.

(Laughter.)

DR. TALAMINI: Dr. Fisher.

DR. FISHER: So Dr. Talamini asked me earlier if there was a Class II device that had special controls asking for clinical data, and yes, there are devices out there. One of the ones that's out there is the HIFU devices for the treatment of ablation of prostate tissue.

So I want to get back to a point that Dr. Martens made a little bit earlier and kind of explain a little bit about special controls. So with the surgical mesh instrumentation, we weren't asking for clinical data as a special control, but that doesn't mean that FDA cannot ask for clinical data. So if there was a situation and if there was a design change where we felt that we needed to see clinical data, we could and would ask for clinical performance data.

Now, the difference is that gives us the flexibility of deciding when we feel it's needed, okay? In this situation we're suggesting that there be clinical performance data as a special control to mitigate risks, and that means that if you all agree that clinical performance data should be considered as a special control, that means that anybody

who comes in with one of these devices would be required to submit clinical performance data with that. It's not our decision. It would be a special control, and there would be an expectation that the sponsor would be providing that information. So I hope that provides a little bit of clarification between the two situations.

DR. TALAMINI: It does. And I'd like to ask the first clarification question. Talamini, Panel Chair.

Help us a little bit with thinking about Class II versus Class III for something like this. Was that just a slam dunk for the FDA that this would be a Class II device? What goes into that thinking? Does the fact that it's already being used on the market go into that thinking? Help us with that a little bit.

DR. FISHER: Okay, I'll take the first shot at this, and then I will ask Dr. Carolyn Neuland to come up and provide some additional clarification if it's needed.

So these devices were preamendment devices, and when they were first classified, they were classified for blood banking purposes, and that went to CBER, okay, the Center for Biologics. And originally it was considered to be a Class III device, okay? So soon after that, when we started getting submissions for something that wasn't blood banking, we said okay, this is what we consider to be a therapeutic indication, and because of that, we feel that it doesn't really fall under the reg that CBER had. So that therapeutic use became an -- it became an unclassified device, okay? So that's why we're here, we're here to classify this.

So we've been working with these devices for over 40 years, and we have been reviewing them with 510(k)s, okay, so as if they were Class II devices, but we've been

asking for clinical data for these. Now, I believe in 2007 CBER took -- and I want to make this point that the devices that CBER uses and the devices that are used for the therapeutic indications, they're basically the same device that work under the same principles, okay? It's centrifugation. They took theirs to panel in 2007, and they down-classified them from Class III to Class II devices.

DR. TALAMINI: Okay.

DR. FISHER: So when it came time for taking this to classification, we took all of this into consideration, how we've been looking at these, how we've been regulating these, what kind of information we have been asking for for sponsors, and we took that all into consideration when we got into the risk mitigations as well as what we felt were necessary special controls. So I hope that provides a little bit of clarification as to kind of our thinking behind this and how we've come up with this strategy.

DR. TALAMINI: Thank you. That is extremely helpful.

Dr. Martens, a clarification question?

DR. MARTENS: Yeah. Dr. Mariani, thank you for the nice presentation. My question is the -- and I think your proposed controls are fine. However, you mentioned there were 17 approvals in the past, 8 recalls on 3 devices, and 40 out of 46 injuries from one manufacturer. Is there a possibility that the design of these devices is so different that there's an unsafe device that is out there? Or was it withdrawn or was it a reclassification of the injury, so there wasn't a problem with that one manufacturer?

DR. MARIANI: As a clarification, there are currently four or five companies that market these devices. So when you get a number of events, it's usually from one device,

and then an update is done to the device to mitigate that risk internally, and we review that as 510(k).

What was the other part of your question?

DR. MARTENS: You know, we're going to be asked to evaluate the adequacy of the proposed controls, and I'm wondering, is there such variation in devices that we really need to look carefully at the controls? Are they able to evaluate design flaws that could cause 40 injuries, 40 out of 46 injuries?

DR. FISHER: So the slide that dealt with the injuries -- and I might be able to get Dr. Hurst up to provide some additional clarification if it's needed. For the 46 injuries, there was an asterisk there because it turned out that the majority of the reporting was done by one company kind of as a catch-up for lack of reporting that they felt was necessary. And when we looked at some of the MDRs, that was -- it was classified as injury, but I'm not sure that all of them would have qualified as injury. They were just -- that's how they were reported out.

As to the devices themselves and the similarities and the differences in the devices, all of these devices work through a very similar mechanism of centrifugation of the blood cells and separation. I think that where you see the differences in the devices are with the ancillary blood sets, the lines, the tubing lines, and the sets that go with them. And I'm going to ask Dr. Frank Hurst if I'm missing anything there.

DR. HURST: Hi, I'm Frank Hurst. I am a medical officer with the reviewing branch.

The only thing I would add in terms of the number of MDRs is that one device certainly has the market share. So the bulk of the MDRs were for that device. But

otherwise, I agree with what Dr. Fisher said.

DR. TALAMINI: Other clarification questions?

Dr. Carson.

DR. CARSON: I can understand how all the recommendations made I totally agree with, but there's one thing that I'm concerned about now, that this is being used actually in patients. Is the performance over time and as well as the performance over use, is there any -- like, I don't know, would there be the same function after using 2 years in two -- over a length of time in 2 patients over 2 years or maybe 1,000 patients in 6 months, with the actual performance of the device? And are risks different and do you -- is there some mechanism that FDA has to evaluate performance data over time or use? Time or use.

DR. HURST: Hi, Frank Hurst again.

I mean, I think it's an excellent question. Just to make sure I understand completely, I think you're asking about sort of the mechanical durability of the physical device; is that correct?

DR. CARSON: Well, there are many parts to this device, right? So I'm not so concerned about the disposables because -- but the actual centrifuge. I mean, maybe after a year it removes a whole lot more red blood cells than we think, or it allows more air to put patients at risk for embolus, just because it's older or it's used more.

DR. HURST: I think that's a great point, and we can certainly look to incorporate that into the performance testing that's required.

DR. CARSON: I think when it was used for biologics, they could look at the

outcome of the blood and the blood separation. They had an easy outcome measure. But now, I mean, your information was really quite important. Now there's something else besides. There's the patient that's now exposed to the function.

DR. TALAMINI: So you're asking a lifecycle durability type question?

DR. CARSON: Yeah.

DR. TALAMINI: Yeah.

DR. FISHER: Ben Fisher, FDA.

You know, I think we're faced with that with any device. You know, I'm just thinking of -- you know, because scopes are a big issue and some of the infections and -- you know, is it the same thing if you used the same scope twice or if you use four different scopes or if you use one scope four times? And yeah. So, you know, I hear what you're saying, and I think that that's something that we can take back for consideration.

The other thing that you were saying, though, is that this involves a patient. And you also have to realize that blood banking also involves a patient, because even though we're going to do a separation and in our situation it's going to be returned back to the patient, even in the case of blood banking, there's going to be a separation of components, and those are going to still go into another patient, okay, just not immediately.

DR. CARSON: Right, but those are measurable.

DR. FISHER: Exactly. And there are tests that could be performed on those in between, correct, to my understanding.

DR. TALAMINI: Dr. Hicks.

DR. HICKS: I want to ask again about the correlation between the information you've obtained over thousands and thousands of patients for dialysis in this. There's some similarity to them. Are there things that you've learned from dialysis that you need to look at in this group?

DR. HURST: Hi, Frank Hurst again.

Yeah, I think that's an excellent point, and we actually did use the special controls for dialysis machines to inform the special controls for these devices.

DR. TALAMINI: Yes?

DR. NEULAND: Hi, I'm Carolyn Neuland. I am the Branch Chief of the Renal Devices Branch that oversees the review of these devices.

And just to let you know, and it may have been on Margie Shulman's slide, but the hemodialysis equipment is regulated as a Class II device with special controls, and it is very similar testing that these two are doing. If you do think there's a durability bench mechanical testing that would be important to add as a special control, we can add that. It could go under our functional testing. That was to address your question earlier. I mean, there is durability testing done on all of these machines when they're manufactured. But whether it goes out long enough would be the question, and we can look into that a little bit more.

DR. CARSON: My question was really almost general for FDA. I didn't know about durability testing, and it seems to me that this particular device might be something that it is important to look at durability over time and over use.

DR. NEULAND: Um-hum. That's a very good point.

DR. TALAMINI: Other clarification questions?

Dr. Hicks.

DR. HICKS: Just on the one company that had the 45 issues there that were sent in, when you broke those down, I mean, are they issues -- mechanical issues? Are they all mixed together? Operator error? Are they patient related and some with the patient?

DR. HURST: Yeah, they're all mixed together. There's a table in the Executive Summary that categorizes them all, and I don't have it in front of me, but they sort of span the lists of risks that were provided. You know, it could be that the patient had perioral numbness related to, you know, presumed hypoglycemia from citrate toxicity during a device. It could be that the disposable separated, resulting in blood loss. So it does widely span the list of risks.

DR. TALAMINI: This is Talamini.

Is it fair to say that that number doesn't concern the FDA because of this catch-up issue and because of the market penetration of that particular company? Is that a fair statement?

DR. HURST: That is a fair statement. Again, we individually reviewed each of those and did not believe that the risks were different than the ones that were not placed into that category.

DR. TALAMINI: Okay. Any other clarification questions?

(No response.)

DR. TALAMINI: Thank you, FDA.

So from a process point of view, to address this question directly for the Panel, it is

essentially going to be to go back through that exact presentation with a specific answer at the end of each large portion. So maybe once again we could break this down and ask the general question of the Panel, whether the Panel is comfortable with this, in general, as a Class II device with specific conditions sort of as described, or is there a Panel member with an appetite for this to be a Class III or a Class I device?

Yeah, Dr. Hicks.

DR. HICKS: Could Dr. DePalma make a comment now before we go down that road?

DR. TALAMINI: I was actually going to ask him to do that after we sort of get that big, big question out of the way, but we can go either direction. If you want to comment first, that's great.

DR. DePALMA: Yeah. I mean, if I have this right.

UNIDENTIFIED SPEAKER: You're good as long as the red light is on.

DR. DePALMA: Here we go. So, you know, I have a significant amount of clinical experience in therapeutic apheresis, both as a fellow at the NIH and then at GW, and these are time tested. So there's a lot of literature. The American Society of Apheresis has come out many years ago with specific categories in which certain diagnoses carry sort of the proof of effectiveness of therapeutic apheresis and some categories where it's not recommended. I feel comfortable with this being a Class II device with those general and special controls in place.

However, the question regarding durability of performance is an excellent one, not only as a general question for devices but in particular this instrument. For example,

many of these devices have maintenance contracts with the manufacturer, and I'm pretty sure that they do therapeutic -- they do testing on a periodic basis looking at the biophysical parameters of the device, flow characteristics, centrifugation speeds. I mean, all of those are necessary to optimize in order for you to get effective separation. So I believe that all of that would flow -- no pun intended -- through those contractual agreements. I don't think that there's any institution that would use these devices without such a contract and determination of performance characteristics indefinitely.

DR. TALAMINI: Thank you.

So I'll go back to the Class I and Class III versus Class II with special controls. Are there any Panel members that would want to make a case or argue for something other than what the FDA has proposed, which is Class II with special controls?

(No response.)

DR. TALAMINI: Okay, seeing none, so that gets us then to the specifics really of the special controls. You've seen them in the presentation. We've had one substantial potential issue addressed in terms of lifecycle and durability. Are there others that we want to deliberate before directly answering the set of questions for the FDA?

Dr. DePalma, in particular, as our expert, we'd love to hear more from you, if you have thoughts.

DR. DePALMA: Well, I can only say that these devices provide lifesaving and life-sustaining characteristics in the appropriate groups of recommended diagnoses. They're time tested. There's vast literature. So I feel that this is an appropriate classification with the appropriate special controls in place. Whether there needs to be specific wording

from the FDA with regards to maintenance contracts or periodic testing of performance, I'd leave that up to the FDA. I believe that's largely in place, but whether that needs to be monitored and enforced or not, I couldn't really comment on that specifically.

DR. TALAMINI: Thank you.

And, Dr. Fisher, with respect to the clinical data collection issue that you brought up, did you bring that up because it is specifically referenced in these questions, or as a more general --

DR. FISHER: No, it was more a general comment and that, you know, I thought it was going to be the elephant in the room, in that, you know, you're asking for it here, but you didn't ask for it before. So why? So I just wanted to kind of explain what the difference of this situation was and to address Dr. Martens' comment about that we -- even though it wasn't listed for the surgical instrumentation, that we could ask for it if we needed it.

DR. TALAMINI: Okay. So if you look at Question 1 and the list of risks that are there, any Panel members see one on the list that should be removed or have a risk in mind that is not on the list for these devices? And in parallel, the risk mitigation measures on the following page, which correspond to each of these risks, sort of peruse that briefly and see if there are any that we should deliberate before directly answering this question for the FDA. It is a long list. I'll give you just a minute.

Yeah, Dr. Hicks.

DR. HICKS: I want information from Dr. Fisher. During the process of the FDA producing this document, they said it was the National Association of -- do you in any way

question and ask, you know, for their thoughts about anything or concerns? Is this all in-house?

DR. FISHER: So is the question, did we specifically reach out to the apheresis society to get information on this?

DR. HICKS: Correct.

DR. FISHER: No, we did not. But it is usually -- the professional societies are the ones who usually come out with the statements on the appropriate uses for devices. And so we are aware of their recommendations for this, for these devices.

DR. HICKS: Okay.

DR. TALAMINI: Well, hearing no calls for additions, subtractions, or modifications, I think the Panel is probably ready to directly answer the question for the FDA. So why don't we go ahead to the specific questions?

MR. ANTONINO: Mark Antonino again.

The first question to the Panel is related to the completeness of identified risks to health for centrifuge-type apheresis devices. FDA has identified the following risks to health:

- Thrombosis in patient and device which can include clotting of the extracorporeal circuit, vascular access clotting, or clotting to other blood vessels.
- Adverse tissue reaction which can result from the use of device components that are not biocompatible. The risk also includes allergic reactions, which can be reactions to device materials or reactions to blood products used

with the device.

- For the identified risks of infection and pyrogen reactions which includes febrile reactions, inflammatory response syndromes, infection, sepsis, and microbial contamination.
- Device failure/disposable failure which includes injury resulting from failure of one or more of the device components.
- Air embolism which occurs if air enters the circuit and subsequently the bloodstream, which can result in occlusion of small blood vessels resulting in stroke and myocardial infarction.
- For the identified risks of hemolysis which includes damage to red blood cells with subsequent release of cellular contents resulting from the mechanical processing of blood.
- Blood loss/anemia which includes blood leaks from the circuit, loss of blood from a discarded extracorporeal circuit after clotting, or increased risk of bleeding from anticoagulation medications or removal of clotting factors during therapy.
- Toxic reaction to anticoagulant which can include citrate toxicity, which is typically manifested by hypocalcemia and alkalosis.
- For the identified risk of electrical shock hazard which can include electrical burns and cardiac arrhythmias.
- Fluid imbalance which can result in hypovolemia or fluid overload.
- Inadequate separation of blood components which involves the unintended

removal of blood components.

- And lastly operator error in which incorrect use of the device can lead to additional clinical risks.

Please comment on whether you agree with the inclusion of all of the risks in the overall risk assessment of the centrifuge-type therapeutic apheresis devices.

In addition, please comment on whether you believe that any additional risks should be included in the overall risk assessment of centrifuge-type therapeutic apheresis devices.

DR. TALAMINI: Thank you.

Dr. Iglesia, do you want to begin? And we'll go to your right.

DR. IGLESIA: This is Cheryl Iglesia.

I agree and maybe just add something about the maintenance durability issue.

DR. TALAMINI: Thank you.

Dr. DePalma.

DR. DePALMA: I agree, and I would echo what my colleague just stated.

DR. TALAMINI: Thank you.

Dr. Donatucci.

DR. DONATUCCI: I agree.

DR. TALAMINI: Dr. Fennal.

DR. FENNAL: I agree.

DR. TALAMINI: Dr. Martens.

DR. MARTENS: I agree. I read the references on my way down and the risks seem

-- the list seems very comprehensive. I also thank Dr. Mariani for giving me the clarification, and Dr. Fisher also, the clarification of the injuries. I think they're included here, and this is complete.

DR. TALAMINI: Thank you.

Dr. Efron.

DR. EFRON: I agree.

DR. TALAMINI: Dr. Hicks.

DR. HICKS: Agree.

DR. TALAMINI: Dr. Afifi.

DR. AFIFI: Agree.

DR. TALAMINI: Dr. Carson.

DR. CARSON: Agree.

DR. TALAMINI: Dr. Faulx, on the phone.

DR. FAULX: I agree.

DR. TALAMINI: Great. So, Dr. Fisher, with respect to Question 1, the Panel agrees.

DR. FISHER: Thank you.

DR. TALAMINI: Question 2.

MR. ANTONINO: The second question to the Panel is related to classification.

Section 513(g) of the Food, Drug, and Cosmetic Act states that a device should be Class III if:

- insufficient information exists to determine that general controls are sufficient to provide reasonable assurance of its safety and effectiveness or

that application of special controls would provide such assurance, and

- the device is life-supporting or life-sustaining, or for a use which is of substantial importance in preventing impairment of human health, or if the device presents a potential unreasonable risk of illness or injury.

A device should be Class II if:

- general controls by themselves are insufficient to provide a reasonable assurance of the safety and effectiveness, and
- there is sufficient information to establish special controls to provide such assurance.

And a device should be Class I if:

- general controls are sufficient to provide reasonable assurance of the safety and effectiveness, or
- insufficient information exists to:
    - determine that general controls are sufficient to provide a reasonable assurance of the safety and effectiveness, or
    - establish special controls to provide such assurance, but
        i. is not purported or represented to be for a use in supporting or sustaining human life or for a use which is of substantial importance in preventing impairment of human health, and
        ii. does not present a potential unreasonable risk of illness or injury.

FDA believes general controls by themselves are insufficient to provide reasonable

assurance of the safety and effectiveness, and sufficient information exists to establish special controls to adequately mitigate the risks to health and provide a reasonable assurance of device safety and effectiveness for this device type. As such, FDA believes that Class II is the appropriate classification for centrifuge-type therapeutic apheresis devices. The following slide shows a risk/mitigation table which outlines the identified risks to health for this device type and the recommended controls to mitigate the identified risks.

This table shows the identified risks which have been discussed throughout the presentation. FDA believes that special controls can be put into place addressing each of these risks and provide reasonable assurance of device safety and effectiveness.

For the risk of thrombosis in patient and device, the recommended mitigation measures are performance testing, sterility, labeling, and clinical performance testing.

For the risk of adverse tissue reaction, the recommended mitigation measures are biocompatibility, sterility, expiration date testing, and labeling.

For the risk of infection and pyrogen reactions, the recommended mitigation measures are performance testing, sterility, expiration date testing, and labeling.

For the risk of failure of the device or disposables, the recommended mitigation measures are performance testing, expiration date testing, and labeling.

For air embolism, the recommended mitigation measures are performance testing and labeling.

For the identified risk of hemolysis, the mitigation measures are performance testing and labeling.

For the identified risk of blood loss or anemia, the mitigation measures are performance testing and labeling.

For toxic reaction to anticoagulant, the mitigation measures are performance testing, labeling, and clinical performance testing.

For the risk of electrical shock, the recommended mitigation measures are performance testing and labeling.

For the identified risk of fluid imbalance, the recommended mitigation measures are performance testing, labeling, and clinical performance testing.

For inadequate separation of blood components, the mitigation measures are performance testing and clinical performance testing.

And lastly, for operator error, the mitigation measures are usability performance testing and labeling.

Please discuss whether the proposed special controls appropriately mitigate the identified risks to health and whether additional or different special controls are recommended.

a. The patient-contacting components of the device must be demonstrated to be biocompatible.
b. Performance data must demonstrate that the device performs as intended under anticipated conditions of use as follows:
    - Functional testing must demonstrate:
        - mechanical integrity of the device and disposable;
        - device functionality in terms of separation and removal of

blood components;

- device functionality in terms of fluid and anticoagulation management when the device is used according to its labeling;
- proper functionality of device safeguards and alarms.

This slide shows the continuation of performance data which must demonstrate that the device performs as intended under anticipated conditions of use.

- Mechanical hemolysis testing must be conducted.
- A system-level hazard analysis must confirm that the device does not perform in an unexpected and/or unsafe manner.
- Software verification and validation testing must be performed.
- Appropriate analysis and nonclinical testing must be conducted to validate electrical safety.
- Appropriate analysis and nonclinical testing must be conducted to validate electromagnetic compatibility, or EMC, testing.
- Performance data must demonstrate sterility of the device.
- Performance data must support the shelf life of the device for continued sterility, package integrity, and functionality over the requested shelf life.

c. Device labeling must include the following:

- A description of the device and individual device components; accessories that need to be used with the system, operational

parameters, and software version;

- A description of the pretreatment, performance, and post-treatment steps needed to safely perform each therapy mode;
- A description of the alarms included in the system, the alarm format the suspected cause of the alarm condition, and how the user must respond to the alarm;
- Detailed instructions for the user to properly clean, disinfect, and maintain the device;
- A detailed summary of the device-related and procedure-related complications pertinent to the use of the device.
- In addition, labeling must include a detailed summary of the device-related and procedure-related complications pertinent to the use of the device;
- A summary which describes the possible susceptibility to electromagnetic interference and possible electrical hazards associated with the use of the device; and
- A troubleshooting guide for users to reference if problems are encountered.

d. Clinical performance testing must demonstrate that the device performs as intended under anticipated conditions of use and document any adverse events observed during clinical use.

Please discuss whether you agree with FDA's proposed classification of Class II with

special controls for centrifuge-type therapeutic apheresis devices. If you do not agree with FDA's proposed classification, please provide your rationale for recommending a different classification.

DR. TALAMINI: So we actually should stop before that Panel question because everything before that was No. 2. So we need to put No. 2 to rest. Is the long list of risks and their mitigations correct, or do you have modifications to it? Let's start with Dr. Efron.

DR. EFRON: It is correct. I agree.

DR. TALAMINI: Let's go around this way.

Dr. Hicks.

DR. HICKS: Correct.

DR. TALAMINI: Dr. Afifi.

DR. AFIFI: I agree with it.

DR. TALAMINI: Dr. Carson.

DR. CARSON: Correct.

DR. TALAMINI: Dr. Iglesia.

DR. IGLESIA: Correct.

DR. DePALMA: Correct.

DR. TALAMINI: Dr. DePalma.

DR. DONATUCCI: Correct.

DR. FENNAL: Correct.

DR. MARTENS: Correct.

DR. TALAMINI: Yeah. And Dr. Faulx, on the telephone.

DR. FAULX: Correct.

DR. TALAMINI: Okay. So, Dr. Fisher, the Panel agrees, given the previous discussions with this list.

DR. FISHER: Thank you.

DR. TALAMINI: And then Panel Question 3, which we've already read, but maybe you could just read it again so it's fresh.

MR. ANTONINO: Please discuss whether you agree with FDA's proposed classification of Class II with special controls for centrifuge-type therapeutic apheresis devices. If you do not agree with FDA's proposed classification, please provide your rationale for recommending a different classification.

DR. TALAMINI: So this is the Class II question.

Dr. DePalma, do you want to begin the Class II?

DR. DePALMA: Yes, I believe indeed that's appropriately classified in the Class II category.

DR. TALAMINI: Thank you.

Dr. Donatucci.

DR. DONATUCCI: I agree.

DR. TALAMINI: Dr. Fennal.

DR. FENNAL: Agree.

DR. TALAMINI: Dr. Martens.

DR. MARTENS: I agree.

DR. TALAMINI: Dr. Efron.

DR. EFRON: I agree.

DR. TALAMINI: Dr. Hicks.

DR. HICKS: Agree.

DR. TALAMINI: Dr. Afifi.

DR. AFIFI: Agree.

DR. TALAMINI: Dr. Carson.

DR. CARSON: Agree.

DR. TALAMINI: Dr. Iglesia.

DR. IGLESIA: Agree.

DR. TALAMINI: And Dr. Faulx.

DR. FAULX: Agree.

DR. TALAMINI: So, Dr. Fisher, the Panel agrees with the Class II classification.

DR. FISHER: Thank you, Dr. Talamini, and thank you to the Panel.

DR. TALAMINI: So a comment from our Consumer Representative, Dr. Fennal?

DR. FENNAL: Thank you so much for the privilege to serve. It's been a pleasure to be here with you. I hope I have an easier time getting home than I did getting here.

(Laughter.)

DR. TALAMINI: Agree. Dr. Donatucci.

DR. DONATUCCI: Thank you. And no further comment.

DR. TALAMINI: Terrific. So I think that completes our work for the day.

Dr. Fisher, do you have final comments?

DR. FISHER: Dr. Talamini and the other Panel members who served for both days, I thank you very much for your tolerance with all the travel delays and everything that you faced getting here. But I sincerely thank you for your participation and all of your comments. For those who just joined us today, I'd like to thank you for your comments and your service. We couldn't do this without you. For Dr. Mariani, who gave the last presentation, for the record, I'd like her to know that we did not forget that today is her birthday. So happy birthday to her.

And with that, thank you very much, Dr. Talamini.

DR. TALAMINI: Thank you. And I would like to thank all of the FDA presenters and Dr. Fisher for helping us out. I want to thank Lieutenant Commander Garcia for a great job for 2 days. And particularly the Panel. Again, you guys, you focused and you thought through the issues clearly, and we're very grateful for your work and your participation here.

So with that, we will pronounce the second session of the February 25th and 26th, 2016 panel meeting of the Gastroenterology and Urology Devices Panel adjourned. Bye.

(Whereupon, at 12:00 p.m., the meeting was adjourned.)

C E R T I F I C A T E

This is to certify that the attached proceedings in the matter of:

GASTROENTEROLOGY AND UROLOGY DEVICES PANEL

February 26, 2016

Gaithersburg, Maryland

were held as herein appears, and that this is the original transcription thereof for the files of the Food and Drug Administration, Center for Devices and Radiological Health, Medical Devices Advisory Committee.

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CATHY BELKA

Official Reporter