UNITED STATES OF AMERICA

FOOD AND DRUG ADMINISTRATION

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CENTER FOR DEVICES AND RADIOLOGICAL HEALTH

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MEDICAL DEVICES ADVISORY COMMITTEE

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GENERAL AND PLASTIC SURGERY DEVICES PANEL

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October 27, 2022

9:00 a.m. EST

Chairperson

Hobart W. Harris, M.D., M.P.H.
Professor of Surgery
Division of General Surgery, UCSF — San Francisco, CA

Attendees

Karla V. Ballman, Ph.D.
Division Chief of Biostatistics & Epidemiology
Cornell Medicine — New York, NY

Mary H. McGrath, M.D., M.P.H.
Professor of Surgery
Division of Plastic Surgery, UCSF — San Francisco, CA

Susan Galandiuk, M.D.
Professor of Surgery
Division of Colorectal Surgery, University of Louisville — Louisville, KY

Michael DeLong, M.D.
Assistant Professor-in-Residence, Division of Plastic Surgery, UCLA — Los Angeles, CA

Stephen Li, Ph.D.
Biomedical Scientist, Li Consulting — Palm Harbor, FL

Gordon H. Baltuch, M.D., Ph.D.
Neurosurgeon, Columbia Neurosurgery (New York, NY)

Sandra Agazie, R.N., BSN, CMSRN
Chief Executive Officer, Sanzie Healthcare Services, Inc. — Fayetteville, GA

Fernando Diaz, M.D., Ph.D
Chair, Dept. of Neurological Surgery, Oakland University School of Medicine and William Beaumont Hospitals (Southfield, MI)

Byron G. Thompson, Jr., M.D.
Professor, Department of Neurosurgery, University of Michigan School of Medicine (Ann Arbor, MI)

Stavropoula Tjoumakaris, M.D.
Professor of Neurological Surgery and Radiology, Director, Endovascular Surgery & Cerebrovascular Neurosurgery Fellowship, Thomas Jefferson University Medical College (Philadelphia, PA)

Jason L. Cormier, M.D.
Neurosurgeon, Acadiana Neurosurgery (Lafayette, LA)

Mary Olivera, M.S., C.R.C.S.T

President & CEO, OSPECS Consulting, LLC (Newburgh, NY)

Matthew Bloom, M.D., M.S., F.A.C.S.
Trauma and Emergency General Surgery, Critical Care, Cedars-Sinai Medical Center (Los Angeles, CA)

Renata Block, M.M.S., PA-C
Physician Assistant, Advanced Dermatology & Aesthetic Medicine (Chicago, IL)

Sandra Agazie, R.N., BSN, CMSRN
Chief Executive Officer, Sanzie Healthcare Services, Inc. (Fayetteville, GA)

Industry Representative
P. LaMont Bryant, Ph.D.
Vice President of Regulatory Affairs
Ethicon, Inc.; Johnson & Johnson

Consumer Representative
Rachel S. Brummert
Founder, Quinolone Vigilance Foundation

Patient Representative
Sonia Morris
Adult Cancer Patient Advocate (Mount Juliet, TN)

Food and Drug Administration

Heather Dean, Ph.D.
U.S. Food & Drug Administration, CDRH — Silver Spring, MD

David Krause, Ph.D.
U.S. Food & Drug Administration, CDRH — Silver Spring, MD

Binita Ashar, M.D.
U.S. Food & Drug Administration, CDRH — Silver Spring, MD

Long H. Chen, Ph.D.
U.S. Food & Drug Administration, CDRH — Silver Spring, MD

Designated Federal Officer

Candace Nalls

Food and Drug Administration Presenters

Frances Wilder, Ph.D. — Medical Device Classification Process
Regulatory Advisor, Regulation, Policy, and Guidance (RPG)

Meixia Bi, Ph.D. — Classifying nail prostheses under product code MQZ
Biologist, Lead Reviewer, CDRH/OPEQ/OHTIV/DHTIVB

Rachel Thomas, Ph.D. — Classifying ultrasonic surgical devices regulated under product codes LFL, NLQ and LBK
General Engineer, CDRH/OPEQ/OHTV/DHTVA

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CALL TO ORDER

Dr. Harris: Good morning, I would like to call this meeting of the General and Plastic Surgery Devices Panel to order. I am Dr. Hobart Harris, the chairperson of this panel and I am located at the University of California in San Francisco. I note for the record that the voting members present constitute a quorum as required by 21 CFR Part 14. I would also like to add that the panel members participating in today's meeting have received training in FDA device law and regulations.

For today's agenda, the panel will discuss and make recommendations on the classification proposals for nail prostheses, ultrasonic surgical instruments, single use reprocessed ultrasonic surgical instruments, and neurosurgical ultrasonic instruments.

INTRODUCTIONS

Before we begin, I would like to remind the public and panelists that this is a non-voting meeting and ask our distinguished committee members and FDA attending virtually to introduce themselves. Committee members, please turn on your video monitors if you have not already done so and unmute your microphones before you speak. I will call your name; please state your position, affiliation, and area of expertise. Dr. Karla Ballman.

Dr. Ballman: Hi, I'm Karla Ballman. I am a Professor and the Division Chief of Biostatistics at Weill Cornell Medicine in New York, and my area is biostatistics.

Dr. Harris: Thank you. Dr. Mary McGrath.

Dr. McGrath: Good morning. I'm Mary McGrath, and I am a plastic surgeon. My position

is a Professor Emerita at the University of California, San Francisco.

Dr. Harris: Thank you. Dr. Susan Galandiuk.

Dr. Galandiuk: Yes, I am a Professor of Surgery at the University of Louisville. I'm a colorectal surgeon.

Dr. Harris: Thank you. Dr. Michael DeLong.

Dr. DeLong: I'm Mike DeLong, I'm an assistant Professor in Plastic Surgery at UCLA, and my research interests are medical devices and regulatory science.

Dr. Harris: Thank you. Dr. Stephen Li. I'm sorry, Dr. Li, you need to unmute. You're muted, Dr. Li.

Dr. Li: I apologize, my button doesn't always seem to click. I'm Stephen Li. I am at an independent laboratory in Tampa, Florida. My areas of expertise are bioengineering and biomedical materials.

Dr. Harris: Thank you. Dr. Gordon Baltuch.

Dr. Baltuch: Gordon Baltuch. I'm a surgeon and professor at Columbia University. My area of expertise is deep brain stimulation and focused ultrasound.

Dr. Harris: Thank you. Dr. Stavropoula Tjoumakaris?

Dr. Tjoumakaris: I am Stav Tjoumakaris. I'm a professor of neurosurgery at Thomas Jefferson University and fellowship director for cerebrovascular. My area of expertise is endovascular and cerebrovascular neurosurgery.

Dr. Harris: Thank you. Dr. Jason Cormier.

Dr. Cormier: Yes, Jason Cormier. I'm a neurosurgeon here in Lafayette, Louisiana. I'm the director of neurosurgery at Lafayette Surgical Hospital. I'm the director of neurovascular and supravascular surgery at Our Lady of Lourdes Hospital in Lafayette. My areas of expertise are intracranial surgery, including tumors and vascular lesions.

Dr. Harris: Thank you. Mary Olivera.

Dr. Olivera: Good morning. I am an independent consultant for OSPECS Consulting and director of sterile processing. My area of expertise is reprocessing and sterilization of reusable items.

Dr. Harris: Thank you. Dr. Matthew Bloom?

Dr. Bloom: Good morning. I'm Matthew Bloom, I'm associate professor of surgery at Cedars- Sinai Medical Center in Los Angeles. My area of expertise is trauma surgery.

Dr. Harris: Thank you. Renata Block.

Ms. Block: Good morning. My name is Renata Block, I'm a dermatology physician for – sorry, I am a dermatology physician assistant with almost 20 years of experience. I practice in a private practice here in Chicago, specializing in general dermatology and aesthetic medicine.

Dr. Harris: Thank you. Sandra Agazie.

Ms. Agazie: Good morning. My name is Sandra Agazie, chief executive officer of Sanzie Healthcare Services in Fayetteville, Georgia. My area of expertise is nursing. Thank you.

Dr. Harris: Thank you. Dr. P. LaMont Bryant.

Dr. Bryant: LaMont Bryant, worldwide vice-president, regulatory affairs, Ethicon/Johnson & Johnson. I'm industry representative for the panel.

Dr. Harris: Ms. Rachel Brummert?

Ms. Brummert: Good morning. I'm Rachel Brummert. I am with the American Society of Pharmacovigilance, and I'll be the consumer representative today.

Dr. Harris: Thank you. Ms. Sonia Morris?

Ms. Morris: Hi. I'm Sonia. I'm a volunteer with the Colorectal Cancer Alliance, and my expertise is colorectal cancer survivorship.

Dr. Harris: Thank you. Dr. Heather Dean?

Dr. Dean: Hi. I'm Heather Dean. I am the acting director of the Division of Infection Control and Plastic Surgery Devices.

Dr. Harris: Thank you. Dr. Chen.

Dr. Chen: Good morning. This is Long Chen. I'm the acting director for the Division of General Surgical Devices.

Dr. Harris: Thank you. Dr. David Krause.

Dr. Krause: Good morning, everyone. I'm David Krause. I'm a cell biologist by trade, I'm the – sorry – getting befuddled; it's early here out on the West Coast. I'm the deputy office director for the Office of Surgical and Infection Control Devices. Thank you.

Dr. Harris: Thank you. Candace Nalls, the designated Federal Officer for today's general

and plastic surgery devices panel, will make some introductory remarks.

Ms. Nalls: The Food and Drug Administration, FDA, is convening today's meeting of the General and Plastic Surgery Devices Panel of the Medical Devices Advisory Committee under the authority of the Federal Advisory Committee Act, FACA, of 1972. With the exception of 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 regulation.

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 U.S.C. Subsection 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 of compliance with federal ethics and conflict- of- interest laws. Under 18 U.S.C. Subsection 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 financial conflict of interest.

Related to the discussions 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 purposes of 18 U.S.C. Subsection 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, the panel will discuss and make recommendations on the classification proposals for nail prostheses, which are currently unclassified preamendments devices, to be Class I, general controls; and ultrasonic surgical instruments, single- use reprocessed ultrasonic surgical instruments, and neurosurgical ultrasonic instruments, which are all currently unclassified preamendments devices to be Class II, general and special controls, particular matter of general applicability.

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 U.S.C. Subsection 208.

Dr. P. LaMont Bryant is serving as the industry representative, acting on behalf of all related industry. Dr. Bryant is employed by Ethicon, Inc., a subsidiary of Johnson & Johnson.

We would like to remind members and consultants that if the discussions involve any other products or firms not already on the agenda for which an FDA participant has 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 they may have with any firms at issue.

A copy of this statement will be available for review and will be included as part of the official transcript. Thank you.

For the duration of the General and Plastic Surgery Devices Panel meeting on October

27, 2022, Ms. Sonia Morris has been appointed to serve as a temporary non-voting member.

For the record, Ms. Morris serves as a patient representative, consultant for the Oncologic Drugs Advisory Committee at the Center for Drug Evaluation and Research, CDER.

This individual is a special government employee who has undergone the customary conflict-of-interest review and has reviewed the materials to be considered at this meeting.

The appointment was authorized by Russell Fortney, Director, Advisory Committee Oversight and Management staff, on September 27, 2022.

Before I turn the meeting over to Dr. Harris, I'd like to make a few general announcements. In order to help the transcriber, identify who is speaking, please be sure to identify yourself each and every time you speak. The press contact for today's meeting is Audra Harrison. Thank you very much. Dr. Harris.

Dr. Harris: Thank you, FDA has received no requests to speak during the open public hearing portion of today's meeting. Therefore, we will continue with today's agenda.

I would like to invite FDA to start their first presentation for today. I would like to remind public observers at this meeting that while this meeting is open for public observation, public attendees may not participate except at the specific request of the panel chair. FDA, you may now begin your presentation.

FDA PRESENTATION — Classifying nail prostheses under product code MQZ

Dr. Wilder: Hello, my name is Frances Wilder, and I am a regulatory advisor within CDRH'S Office of Product Evaluation and Quality. I will be providing you with a high-level

overview of the medical device classification process which formed the basis for our discussion during this panel meeting.

The purpose of this panel meeting is to discuss the classification of devices that currently remain unclassified. Specifically, for ten preamendments unclassified device types, the panel will be asked to provide input to the FDA on the appropriate classification for each device type.

FDA categorizes medical devices into three classes based on the regulatory controls necessary to mitigate the risks associated with the device type. Class I devices are only subject to general controls. Class II devices are subject to both general and special controls; and Class III devices are subject to general controls and premarket approval.

These regulatory controls will be discussed in greater detail in the following slides, but the important takeaway here is that a device should be placed in the lowest class whose level of control provides a reasonable assurance of safety and effectiveness.

Now we will go into a bit more detail about each of the classes. Again, Class I devices are those devices for which general controls are sufficient to provide reasonable assurance of the safety and effectiveness of the device. General controls are basic requirements that apply to all medical devices and are outlined in the federal Food, Drug and Cosmetic Act. Some examples of general controls include registration and listing device requirements, following good manufacturing practices, adhering to record keeping and reporting requirements, and ensuring that devices are not misbranded or adulterated. Most Class I devices do not require FDA premarket review prior to being marketed.

On the right-hand side of the slide you can see a few examples of Class I devices, which

include simple gauze wound dressings, manual surgical instruments for general use, and introduction drainage catheters. There is also an alternative pathway to determine that a device is Class I. Class I devices could also be devices that cannot be classified into Class III because they are not life-sustaining, life-supporting, or of substantial importance in preventing impairment of human health, and they do not present a potential unreasonable risk of illness or injury. And these devices cannot be classified into Class II because insufficient information exists to establish special controls to provide a reasonable assurance of safety and effectiveness.

Class II devices are those devices which cannot be classified into Class I because general controls by themselves are insufficient to provide reasonable assurance of the safety and effectiveness of the device; and for which there is sufficient information to establish special controls to provide such assurance. There are many types of special controls, but some examples include performance testing, sterilization validation, and device-specific labeling requirements. These special controls, in combination with the general controls previously described, provide a reasonable assurance of safety and effectiveness for Class II devices.

Examples of Class II devices include surgical sutures, negative pressure wound therapy devices, and laser surgical instruments for general and plastic surgery use. Typically, Class II devices require a premarket notification or a commonly referred to as a 510(k) prior to being marketed in the U.S. Within these 510(k) submissions, companies must also provide evidence demonstrating how the special controls for the specific device type are met.

Class III devices are those which cannot be classified into Class II because insufficient information exists to determine that general and special controls are sufficient to provide reasonable assurance of the safety and effectiveness of the device, and the devices are

life-sustaining or life-supporting or are of substantial importance in preventing impairment of human health, or they present a potential unreasonable risk of illness or injury. Class III devices typically require premarket approval through a premarket approval application, or PMA, prior to being marketed.

Examples of Class III devices include breast implants, dermal implants for aesthetic use, and absorbable hemostatic agents. Here you can see a flow chart which walks through the general decision-making process for device classification. We start with determining whether general controls are sufficient to provide reasonable assurance of safety and effectiveness. And if so, the device can be appropriately regulated in Class I. If not, we ask when there is sufficient information that allows us to develop special controls. If so, the device can be appropriately regulated in Class II. If not, then it would be Class III if the device is life-supporting or life-sustaining, or if it is of substantial importance in preventing impairment of human health, or if it presents a potential unreasonable risk of illness or injury. If the device is not life-supporting or life-sustaining or of substantial importance in preventing impairment of human health and does not prevent a potential unreasonable risk of illness or injury, then we end up back at Class I designation.

Now that we have discussed the general device classification scheme, we will move on to the classification process for the preamendments, unclassified device types, which are the focus of this panel meeting.

For those who are unfamiliar, a preamendments device refers to a device type which was introduced into interstate commerce prior to May 28, 1976, or the date of enactment of the Medical Device Amendments to the Federal Food, Drug, and Cosmetic Act. An unclassified

device is a preamendments device which was not classified by the original classification panels; therefore, no classification regulation currently exists for these devices.

This brings us to the purpose of this panel meeting, which is to formally classify these unclassified devices. Please note that while these devices are not classified, they currently have to be cleared through the 510(k) process prior to being marketed. These preamendments unclassified devices will be classified once the FDA has taken the following steps. First, FDA will solicit input and a recommendation from the device classification panel, which is the purpose of this meeting.

After this meeting, FDA will publish the panel's recommendation for comment, along with a proposed rule outlining FDA's proposed classification for the device. Finally, after taking into account public comments, the FDA will publish a final rule classifying the device. During this panel meeting, we ask the panel to provide input on the classification of these unclassified device types, and whether each should be classified into Class III, Class II, or Class I.

The panel input should include an identification of the risks to health presented by each device type, and a discussion of whether the device is life-supporting/life-sustaining, or of substantial importance in preventing impairment of human health, or if the device presents a potential unreasonable risk of illness or injury. The panel will be asked to discuss whether general controls alone are sufficient to provide reasonable assurance of safety and effectiveness for each device type, and if not, whether sufficient information exists to develop special controls, and what those special controls should be to provide a reasonable assurance of safety and effectiveness for the device type.

Following this panel meeting, the FDA will consider all available evidence, which includes the input received from this panel and the public. The FDA will then publish a proposed rule in the Federal Registers, proposing classification of these device types and seeking public comment on the proposal. Finally, FDA will issue a final rule identifying the appropriate class. If FDA determines that the device can be appropriately regulated as Class I or Class II devices, these devices may continue to be marketed. If, however, FDA determines that they fall into a Class III designation, a separate call for PMAs will also be published. Existing devices may remain on the market until a specified date at which point a PMA should be submitted in order to continue marketing the device. If this PMA is not approved, the existing devices would be considered misbranded and must be removed from commercial distribution.

I hope that this has provided you with sufficient background information to set the stage for the forthcoming discussions. Thank you for your time and attention.

Dr. Harris: Thank you. Are there any clarifying questions from any members of the panel regarding that presentation? If so, please use the raise your hand function via the Zoom platform. So if there are no questions, does FDA have questions for the panel at this time, or are we going to move to a next presentation regarding the devices to be considered today?

Dr. Dean: I believe we can move to the next presentation. Thank you.

Dr. Harris: Great. You may start that now. Thank you.

Dr. Bi: Good morning. My name is Meixia Bi, and I am the lead reviewer in the Division of Infection Control and Plastic Surgery Devices within the Office of Surgical and Infection Control Devices, in CDRH's Office of Product Evaluation and Quality. Today I will be

presenting information regarding efforts to classify nail prostheses and their product code MQZ. This is the outline of my presentation, and these are the items that we will be discussing today.

Nail prostheses are devices intended to temporarily provide structure, for example, splint, brace, to ingrown or damaged nails to correct or support nail growth. In general, nail prostheses are constructed out of polymeric or metallic materials. Ingrown nails, which are predominantly toenails, a prosthesis device which be used to apply outward pressure on each side of the nail between the nail and the surrounding skin and correct nail over curvature. For injured or deformed nails, such as after traumatic injury, which is predominately on fingernails, a nail prosthesis device may be used as a temporary splint for nail bed reconstruction, and then the device is removed. The device can be temporarily sutured in place and subsequently removed once the desired natural healing of the nail has taken place.

A nail prosthesis intended to correct ingrown nails may be suitable for home use, while a nail prosthesis intended for injured or deformed nail bed is intended to be used in surgical settings. The indication for use identifies that there is a condition that the device diagnose, treat, prevent, cure or mitigate, including a description of the patient population for which the device is intended.

Nail prostheses have been cleared devices to correct the shape of overcurved or painful nails without operation. To loosen and give shape to thickened nails, overcurved nails and pincer nails without operation, to restrain the ingrown portion of the nail to grow in a forward motion, thus eliminating the ingrown nail, to splint for reconstruction acute nailbed injuries or other deformities of the nail plate. Nail prostheses are preamendments unclassified device type and have been in commercial distribution prior to May 28, 1976. This means that this device type

was marketed prior to the Medical Device Amendment Act of 1976. It was not classified by the original classification panels. Currently these devices are being regulated through the 510(k) pathway and are cleared for marketing if their intended use and technological characteristics are substantially equivalent to a legally marketed predicate device. Since these devices are unclassified, there is no regulation associated with the MQZ product code.

To date, FDA has cleared three 510(k)'s under the product code MQZ. Ingrown toenails are a common foot condition in people of all ages. The condition may develop in any toenail, but most often occurs in the big toe. An ingrown toenail occurs when a nail grows into the skin along the side of the toe or when the skin on one or both sides of the nail grow over the edges of the nail.

Common symptoms are pain, redness, swelling and infection. The factors leading to ingrown nails include wearing tight shoes, improper grooming and trimming of the nail, trauma, infection, or certain medical or congenital conditions. Trauma to the nail plate and the nail bed, including partial toe or finger amputations, for treatment and healing may be more complicated and may affect both aesthetic experience and functional performance of the nail.

Failure to achieve a clean flat nail bed may result in a poorly attached nail, dystrophic nail, split nail, thickened and discolored nail, and even a short nail with tissue overgrowth. If the nail plate does not grow to the tip of the finger, significant loss of tactile sensation may occur, causing functional debility and compromise the quality of life.

Ingrown toenails may be noticed by the patient at early stage when pain starts. The healthcare provider diagnoses an ingrown toenail based on the visual checking on the affected

toe, the patient's symptoms, and possible causes. No complex examinations are needed.

Some lab tests, such as a blood test may be requested if the doctor thinks an ingrown toe mail has caused other complications. Trauma to a nail plate and the nail bed may require specialized care, including first treating the nail bed injury and any associated soft tissue loss followed by ensuring the proper longitudinal growth of the nail plate across a well-healed, vascularized flat nailbed. Preparing the nailbed may require dermabrasion, excision of scar tissue and tissue grafting and flaps.

In both phases of treatment, using a nail prosthesis or splint is critical to ensure the best cosmetic and functional outcome. Nail prostheses are used for the purpose of preventing nail overgrowth and redirecting nail growth for treatment of ingrown nails. Correction of over-curvature is commonly addressed with surgical techniques to remove the ingrown portion of the nail. Over-the-counter products also correct over-curvature, which include bandage and gel combinations to soften the nail, and the topical products that may soften the nail bed to prevent inward growth of the nail. Patients with over-curvature of nails may also decide not to seek treatment or to try home remedies, such as soaking feet in warm water or applying petroleum jelly to the over-curved nail.

For nails with traumatic injury, where part or all of the nail has been damaged, patients may receive treatment including surgical repair of the finger and nailbed that has received the trauma, wound care and bandaging may be used to support the injured nailbed and surrounding tissue. A damaged or removed nail can also be left to heal on its own.

A systematic literature review was conducted to get any published information regarding

the safety and effectiveness of nail prosthesis under product code MQZ.

The first search for nail prosthesis device that correct the ingrown nails were conducted to identify any relevant articles published between May 1, 1976, and April 1, 2022. A supplemental literature search was conducted to identify literature reporting outcomes related to the use of nail prosthesis devices, such as the Inro Splint between 1976 to July 2022. The searches were limited to human clinical studies with full text available in English.

The first search yielded three records. The supplemental research for Inro splint yielded one article. Therefore, a total of four published literature references, covering four studies, were determined to be relevant to the safety and effectiveness of nail prostheses. For safety assessment, the searches identified literature reporting on the following adverse events related to the use of nail prosthesis devices. First, temporary pain with the treatment of nail braces. Second, nail brace dislocations. Third, minor nail infections. Regarding effectiveness assessment, for ingrown nails, around 4 to 8% of patients experienced a recurrence in nail deformity, and nearly all patients reported pain relief within one day.

For nails with traumatic injury, nail regrowth was observed in 16 nails out of 18 fingers treated with the INRO surgical nail splint.

In summary, the literature search between 1976 to 2022 yielded a total of four literature references that were applicable to evaluating the safety and effectiveness of nail prostheses. The quality of evidence in the reviewed studies was low with very limited generalizability.

The next three slides provide backgrounds information for medical device reports, or MDRs. MDR is a mechanism for the FDA to receive significant medical device adverse events

from both mandatory reporters, that is, manufacturers, importers and user facilities; and voluntary reporters, including healthcare professionals, patients, and consumers.

MDR reports can be used effectively to establish a qualitative snapshot of adverse events for a specific device or device type. To detect actual or potential device problems used in a real world setting or environment, including rare, serious, or unexpected adverse events. Adverse events that occur during long-term device use, adverse events associated with vulnerable populations, off-label use, and user error. Although MDRs is a valuable source of information, this passive system has a number of limitations, such as underreporting of events, potential submission of incomplete, inaccurate, untimely, unverified, or biased data. Incidence or prevalence of an event cannot be determined from this reporting system alone. Confirming whether a device actually caused a specific event can be difficult based solely on the information provided in a given report. MAUDE data does not represent all known safety information for a reported medical device.

On May 24, 2022, a search of the MDRs were conducted. The database was queued for product code MQZ with no date limitation. This search did not identify any relevant MDRs for nail prosthesis devices. The medical device recall database contains medical device recalls classified since November 2002. Since January 2017, it may also include correction or removal actions initiated by a firm prior to review by the FDA. The status is updated if the FDA identifies a violation and classifies the action as a recall, and again when the recall is terminated. FDA classification, and thus the posting date, may occur after the firm recalling the medical device conducts and communicates with its customers about the recall.

The FDA queried the medical device recall database on August 18, 2022, to identify

recalls related to nail prosthesis devices. The search was not time frame restricted and included all recalls reported and their product code MQZ. The search did not identify any relevant recalls for nail prosthesis. To identify the risks of these devices, we had reviewed MDRs, recall information, and literature analysis as previously discussed, and the information available to the FDA regarding cleared devices. Here are the three identified risks for nail prostheses.

The first identified risk is adverse tissue reaction, which can result from the use of device materials that are not biocompatible. Another risk is discomfort with pain or nail breakage, which can result from the device applying too much pressure to the nail. Last, nail infections can result from inadequate cleansing of the nail before application of the prosthesis or from the introduction of microorganisms to the area once the prosthesis is in place.

The FDA proposed that these risks will be sufficiently addressed by general controls, and do not require special controls as part of the medical device regulation process. We recommend that nail prosthesis be regulated as Class I device. Here is our proposed classification regulation for nail prosthesis devices. Part A of the regulation defines a nail prosthesis as intended to temporarily provide structure to ingrown or damaged nails to correct or support nail growth. A nail prosthesis device intended for ingrown nails helps to correct nail over-curvature. A nail prosthesis device intended for injured or deformed nails, such as after traumatic injury, may serve as a temporary splint to physically cover and protect the injured or damaged nailbed during the healing process. A nail prosthesis is not intended for use on infected nails.

Furthermore, we are proposing these devices be classified as Class I exempt devices with general controls. Thank you for your attention. And that concludes my presentation today.

CLARIFYING QUESTIONS

Dr. Harris: Thank you. We'll begin with any clarifying questions from the panel members regarding the content of that presentation. Ms. Block?

Ms. Block: Thank you for that presentation. I have a question for you in regard to who supplies these nail prosthesis. Are they actually applied in the clinic? Or is it something that the public can get over the counter?

Dr. Dean: I believe of the three that we identified, two were available by prescription only, and one was over the counter. That doesn't mean they necessarily get them in the clinic, as you know, but at least those that are prescribed by a clinician, they would have instructions.

Ms. Block: Thank you.

Dr. Harris: Are there any other clarifying questions? Dr. Li? Remind, everyone, please, state your name for the benefit of our transcriptionist.

Dr. Li: Stephen Li. Do these include the use of – I've seen the use of gels that they put on over the missing part of the toenail and they use something like ultraviolet light to cure the gel to make the prosthesis. Would that count in this category or not?

Dr. Dean: No, not from my understanding of the identification. That is not in the scope here.

Dr. Li: And this is maybe a quick, clarifying – I'm not sure if this is the right time for it. It's a clarification of the Class I device. I noticed there was really no description of the materials that are available to use. So, if it's a Class I device, what would the requirement be for the

materials? Can the manufacturer use just about anything or what conditions would need to be satisfied?

Dr. Dean: We're not – I don't believe we're proposing any restriction on the materials. From the presentation you just saw, I believe that these tend to be made of metals or polymeric materials.

Dr. Harris: Okay.

Dr. Krause: This is David Krause. I could add to that. The 21 CFR provides a rationale for when a product like that needs to have a 510(k). So if we do classify them into Class I, it will likely be exempt from review, but if we find one or someone submits an application and the materials are very different from the ones that we've included currently, and consider it to be different enough, the technological differences, we can request that the manufacturer submit a 510(k) if we find it on the market, or if they do submit a 510(k) and we think it's different enough, we can require a De Novo or different type of application.

So, to answer Stephen's question, if the device is very different or the intended use is very different, we can require an application, and then once we get that application, we can decide whether it can be cleared as Class I exempt, or if it requires a De Novo or even a PMA.

So that is something that we can do based on regulations. Does that answer your question, Stephen?

Dr. Li: Yes, thank you.

FDA QUESTIONS

Dr. Harris: Are there any other clarifying questions regarding the content of the presentation? If not, at this time we'll focus our discussion on the FDA questions. Panel members, a copy of these questions is available in your packets. And I would again remind the panel members to identify themselves prior to speaking to facilitate transcription. FDA, will you please show the first question.

Dr. Bi: We will now go through our questions for the panel to discuss.

Question No. 1. The FDA has identified the following risks to health for nail prostheses. This includes adverse tissue reaction, discomfort, pain or nail breakage, and nail infection. Please comment on whether you agree with inclusion of all the risks in the overall risk assessment of nail prostheses under product code MQZ. In addition, please comment on whether you believe that any additional risks should be included in the overall risk assessment of nail prostheses.

Dr. Harris: Thank you. So, the first question for the panel is whether or not they feel these are appropriate risks associated with this device, and whether any should be either removed or added? So, any comments or questions? Renata Block.

Ms. Block: Hi, this is Renata Block, thank you. A couple of concerns. I'm worried about the sterilization. I know you have the nail infection from inadequate cleansing of the nail before application. But how about the prosthesis itself, as far as inadequate packaging, integrity or sterilization?

Dr. Dean: These devices are not intended to be provided sterile or sterilized. They are intended to, as stated in the presentation, provide support, but they're not implanted, and thus no sterilization is required.

Ms. Block: My second question was any adverse tissue reaction from the device materials, and I think Dr. Li kind of brought that up with different types of materials being used. As far as like the data, he didn't see any research found in that, but it's always a concern moving forward. Was this considered as well?

Dr. Dean: We are always concerned about biocompatibility and adverse tissue reaction, is, I believe, one of those potential risks that were listed. If the materials were greatly different from those that we have previously seen and cleared, then as Dr. Krause mentioned, we would require a 510(k) to look at that, and probably want to see some information about the biocompatibility of the device.

Ms. Block: Thank you for the clarification, I appreciate that.

Dr. Harris: Are there any other questions or comments regarding the risks that have been listed to mitigate safety and efficacy effects for these devices?

If not, and no one has suggested either a change or addition or subtraction of the listed risks, then we will present to Dr. Dean the assumption that the committee is unanimous in its support of the proposed risk.

Dr. Dean: Thank you. We appreciate the input. That's sufficient.

Dr. Harris: Thank you. If FDA will now read the second question.

Dr. Bi: Question No. 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 and special controls are sufficient to provide reasonable assurance of its safety and effectiveness, and the device is 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, 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 is not purported or represented to be for use in supporting or sustaining human life or for use which is of substantial importance in preventing impairment of human health, and does not present a potential unreasonable risk of illness or injury.

The FDA does not believe that special controls will be required for nail prostheses under the product code MQZ, and that general controls will be sufficient to provide reasonable assurance of the safety and effectiveness for nail prostheses. As such, FDA believes that Class I is the appropriate classification for nail prosthesis under product code MQZ.

Please discuss whether you agree with FDA's proposed classification of Class I for nail prosthesis. If you do not agree with FDA's proposed classification, please provide your rationale for recommending a different classification. And that's the end of the panel questions for product code MQZ.

Dr. Harris: Thank you. So now I'll open it up for panel deliberations regarding the issue of the proposal that these nail prostheses be regulated as Class I devices.

Any questions or comments from the panel? Dr. Stephen Li.

Dr. Li: Stephen Li, just a quick question. I just wanted to confirm that there did seem to be some of these devices that used hooks or some method of attachment for the temporary fixation. So, I just want to check that when these hooks or these devices fail that there has in fact been no real serious harm or injury to the patient, other than discomfort from obviously maybe having a second procedure, but nothing serious happens. Would that be a correct statement?

Dr. Dean: That would be – you saw on the presentation, there were very, very few MDRs reported in the past several decades. It appears that reports of patient injury and malfunction are very low.

Dr. Li: Thank you.

Dr. Dean: And as you know, there are limitations; not everything is reported. But it does give an indication that we have not seen serious adverse events.

Dr. Li: Thank you.

Dr. Harris: Any other questions or comments? Then Dr. Dean, the committee – Oh, you'd like to make a comment?

Ms. Agazie: I have a question.

Dr. Harris: Ms. Agazie?

Ms. Agazie: Good morning, Ms. Agazie. I was looking at the Table 1, 510(k), those three products that were cleared by the FDA. Under the product K960843, is that a brace or splint? I'm not sure. Is that considered a brace or splint on the prosthesis, stopping growth? Is that

considered?

Dr. Dean: That is a brace. Both braces and splints are included here, and the reason we included both, they have similar intended – or the same intended use and similar materials and there were only three products total. And so these are included under the same product code.

Ms. Agazie: I wasn't sure what it was. Thank you.

Dr. Harris: Thank you. Any other questions or comments? If not, then the panel agrees with the proposal by FDA to regulate these nail prostheses as Class I devices. Is that sufficient, Dr. Dean?

Dr. Dean: Hearing no objection, I will take that as unanimous consent with the proposal that these be Class I devices. Thank you.

Dr. Harris: Thank you. I would now like to invite the FDA to proceed with the next presentation.

FDA PRESENTATION — Classifying ultrasonic surgical devices regulated under product codes LFL, NLQ and LBK

Dr. Thomas: Good morning. My name is Rachel Thomas, and I am a lead reviewer in the Division of Neurosurgical, Neurointerventional and Neurodiagnostic Devices within the Office of Neurological and Physical Medicine Devices in CDRH's Office of Product Evaluation and Quality.

Today I will be presenting information regarding our effort to classify ultrasonic surgical devices regulated under products code LFL, NLQ and LBK. These devices are currently unclassified, and we are looking for your thoughts and recommendations on the appropriate

regulatory classification for these devices.

This is the outline for the presentation. These are the items that we will be discussing today. We are collectively referring to the devices under all three product codes as ultrasonic surgical devices. Ultrasonic surgical devices are handheld tools indicated for use in a wide variety of both open and minimally invasive surgical specialties. These devices generally employ a metal tip oscillating at a frequency of at least 20 kilohertz. Oscillatory mechanical motion of the tip at high velocities and accelerations causes localized tissue heating, fragmentation, and emulsification.

The oscillating tip plus irrigation and aspiration to remove the fragmented tissue are enclosed in a handpiece manipulated by the surgeon. The power to generate the oscillation is supplied from a console which may be operated by a foot pedal or activated on the handpiece. Ultrasonic surgical instruments are regulated under product code LFL, single-use reprocessed versions of LFL devices are regulated under product code NLQ, ultrasonic surgical devices specifically indicated for neurosurgical uses are regulated as neurosurgical ultrasonic surgical instruments under product code LBK.

Devices with neurosurgical indications are commonly used to treat a wide variety of intracranial and intraspinal tumors with some devices reported to remove cysts and abscesses in the brain and spinal cord.

The Indication for Use Statement identifies the disease or condition the device will diagnose, treat, prevent, cure or mitigate, including a description of the patient population for which the device is intended. All devices cleared under product codes LFL, NLQ and LBK are

for prescription use only. Most ultrasonic surgical devices are indicated for use in the fragmentation, emulsification, and aspiration of soft and hard tissues. Some devices may also be indicated for bleeding control or ligation of vessels.

Listed here are additional surgery types referenced in some IFU statements for ultrasonic surgical devices. Devices cleared under product code LBK are specifically indicated for use in neurosurgery.

All three types of ultrasonic surgical devices are preamendments, unclassified device types. This means that these device types were marketed prior to the Medical Device Amendments Act of 1976. They were not classified by the original classification panels. Currently, these devices are being regulated through the 510(k) pathway and are cleared for marketing if their intended use and technological characteristics are substantially equivalent to a legally marketed predicate device. Because these devices are unclassified, there is no regulation associated with the LFL, NLQ or LBK product codes.

LFL and NLQ devices provide patient benefit as surgical tools employed to treat various conditions within each surgical sub-specialty. With any invasive procedure, there are risks both inherent with each specific procedure and with the anesthetic employed to complete the operation. In contrast to a successfully completed surgical operation, surgical misadventures can occur due to numerous circumstances, including surgeon factors such as insufficient training, error in judgment, and error in technique; patient factors such as poor physiology, concomitant illness, complex disease processes and anatomic variations; and instrument factors such as device failures, design flaws and other factors.

Surgical outcomes following the use of LBK devices are based on a combination of parameters including neurological evaluations, functional improvement (e.g., modified Rankin Scale), imaging outcomes (e.g., tumor burden), overall survival, progression-free survival and complication rate, including subsequent surgical interventions and neurologic complications. LBK devices are commonly used in intracranial and intraspinal tumor resection. Each procedure can be assessed using different measures for success of the treatment.

Potential intra-surgical and post-surgical adverse events for intracranial and intraspinal tumor resection using LBK devices include infection, neurological deficits, seizure, hydrocephalus, thermal injury, and leptomeningeal seeding.

The effectiveness of intracranial and intraspinal tumor resection uses of LBK devices is measured by post-surgery tumor recurrence or progression, overall and progression free survival, gross tumor resection, length of surgery and hospital stay, and post-surgical improvement. There are many cleared surgical tools that assist surgeons in completing operations for a wide variety of disease processes and surgical indications that are similar in function to ultrasonic surgical devices. One example is hand-held, hand-powered sharp instruments that are commonly employed by surgeons to divide tissues. These instruments divide tissue but do not require hemostasis which usually requires additional operative sets with a separate set of instruments.

The draw of ultrasonic surgical devices is that the single device can perform both tissue division and hemostasis, thus preserving and promoting economy of motions and can shorten operative times. Neurosurgical ultrasonic surgical devices are considered part of clinical usual care in the United States when fragmentation and aspiration of neurological tissues is desired.

Another currently available alternative to ultrasonic surgical devices are other electrosurgical devices and suture ligation. Surgical hemostasis can be achieved by other electrosurgical devices capable of tissue coagulation as well as suture ligation methods.

Electrosurgical coagulation devices, when employed correctly, can achieve hemostasis faster than suture ligation at the expense of heat generation, which could cause inadvertent tissue damage by thermal spread. Suture ligation requires additional instruments to correctly deploy the suture material at the bleeding site, and generally require more dexterity and skill to use properly. Additionally, the successful deployment of sutures to stop bleeding is generally slower compared to coagulation methods without the risk of inadvertent tissue damage due to thermal spread.

Staplers can be employed for the control and division of larger blood vessels and/or vascular pedicles. However, staplers are not effective for small, more extensive tissue bleeding. Staplers control bleeding by mechanical compression of the vessel walls between the closed staple line. No heat is generated with staplers, thus eliminating tissue damage by thermal spread. However, staplers are more bulky than other hemostatic instruments and are not designed for precision hemostatic control. Inadvertent tissue injury can occur due to errors in deployment and the correct staple height must be utilized based on the tissue thickness for the device to function as intended.

Two separate literature reviews for ultrasonic surgical devices were conducted. The first review was for product codes LFL and NLQ, and the second review was for product code LBK. Both reviews used two electronic databases, Embase and PubMed/MEDLINE, with specific search criteria. The literature review for product codes LFL and NLQ were limited to studies

published from January 1, 2007, to January 1, 2022 and the search terms used were ultrasonic surgical instruments, ultrasonic surgical aspirators and reprocessed ultrasonic surgical instruments.

After a comprehensive literature review, 18 articles were identified that addressed incidents of adverse events with the use of ultrasonic instruments. For ultrasonic surgical devices under product code LBK, the literature review was limited to studies published from January 1, 2010, to September 1, 2020, with a follow up review conducted for additional literature published between September 1 of 2020 to May 13 of 2022. Search terms were limited to ultrasonic or ultrasound devices in the neurological field or neurosurgery with a focus on all central nervous system tumors, including brain and spinal tumors, brain hemorrhage and brain trauma. A total of 16 published literature references were determined to be relevant to the safety and/or effectiveness of neurosurgical ultrasonic surgical devices. There were also 22 articles identified on devices that appeared to be ultrasonic surgical instruments used for neurological indications, but that do not appear to have been cleared under product code LBK. Due to the similarities, FDA is also including information from these comparable devices for a comprehensive assessment of the safety and effectiveness of neurosurgical ultrasonic surgical devices. Additionally, following the supplemental search, two additional publications were considered.

The literature review was used to assess potential adverse events for ultrasonic surgical devices. Within the literature assessed associated with LFL and NLQ devices, pain reported in 14 out of 18 of the studies was the most commonly reported safety outcome, followed by infection rates which were reported in 9 out of 18 studies. Pain was measured inconsistently among the 14

studies, and the results were mixed with some studies reporting statistically significant pain differences when comparing ultrasonic surgical devices to other cutting methods, and others reporting no statistically significant differences.

Infection incidence with the use of ultrasonic surgical devices ranged from 0.7% to 6.5% among the nine studies, and difference in infection rates compared to other cutting devices was not statistically significant in any of the nine studies. Tissue injury was reported in three studies. In one study, hematoma was reported in two of the 40 ultrasonic scalpel patients compared to one of the 40 conventional treatments, which is 5% versus 2.5% with a p-value of 0.62. Mortality was reported in one study with an incidence of 1 out of 237, which is 0.004%. There were no reports of device malfunction or device-related issues to the user or patients.

For LBK devices, the literature articles reported adverse events associated with the use of neurosurgical ultrasonic surgical devices, when used to remove soft and hard tissues during neurosurgical procedures. The reported adverse events include death, leptomeningeal seeding or LMS, thermal injury, meningitis, bleeding, pneumonia, and neurological deterioration with transient or permanent deficits.

The reported adverse events also included complications such as hospital/surgical complications, post--surgery recurrence and progression, second surgery and intra-postsurgical complications and long-term complications. Aside from complications specific to neurological surgery, overall, the evidence suggests that the potential device-related adverse events appear to be consistent with those identified under the more general search of products associated with product codes LFL and NLQ.

LFL and NLQ encompass a wide variety of surgical procedures, and therefore effectiveness outcomes for these product codes were not assessed. Given that these devices are generally surgical tools, the outcomes related to specific surgeries are not particularly influential in the classification decision making for these products. Given the specificity of the LBK product code to neurological surgical uses, in contrast to LFL and NLQ, the literature associated with LBK was also assessed for effectiveness outcomes. Effectiveness outcomes reported in the published literature as potentially associated with LBK devices include gross total resection, length of surgery and hospital stay and overall post-surgery improvement.

Additionally, other use of LBK stimulation eliciting motor response and subcortical mapping in surgery was summarized. Similar outcomes are reported for non-LBK devices. The evidence suggests that overall, these devices are reported to be effective for the removal of soft or hard tissue in the brain and spine.

In summation, LFL and NLQ ultrasonic surgical devices are used in a wide variety of surgical procedures. The most common risks include pain, infection, tissue injury, and hematoma. LBK ultrasonic surgical devices are primarily used for the resection of brain and spinal tumors and are effective in the removal of soft and hard tissues in the brain and spine. Commonly reported risks include death, LMS, thermal injury, meningitis, bleeding, pneumonia, and neurological deterioration with transient or permanent deficits. It should be noted that there was limited data from well-designed clinical studies and most of the evidence was derived from case reports and case studies, which are limited by small sample sizes, no control or comparison group and limited generalizability.

The next two slides provide background information for medical device reports. For the

sake of time, I will not go through this information in detail since it was summarized previously in the presentation for nail prosthesis under product code MQZ. This is a continuation of the medical device report background.

To further contribute to the benefit/risk assessment of ultrasonic surgical devices, the agency reviewed individual medical device reports, MDRs, using the FDA's Manufacturer and User Facility Device Experience, or MAUDE, database. The MAUDE database reviewed for product code LFL from January 1, 2022, to December 31, 2021. 46,673 relevant MDRs were identified. 44,354 malfunction reports, 2,263 serious injury reports, and 56 death reports. Of the 56 deaths reported, 34 did not implicate the device in the death of the patient. Nine were initiated from literature review and 13 were identified as potentially related to the use of the device.

Data was extracted from the 13 event reports that implicated the device in the death of the patient. In one case during a liver dissection, uncontrolled bleeding occurred after using the harmonic scalpel to dissect tissue and the patient died intraoperatively. The remaining 12 narratives detailed that at the time of surgery, the device appeared to seal and cut the tissue and vessels without incidence. The event narrative from two reports detailed bleeding from mesenteric vessels while the harmonic scalpel was used to seal and dissect tissue. The remaining nine event narratives all detailed dissection of gastric vessels that appeared to be sealed and dried during surgery but opened after the patient was transported out of the operating room.

The most common occurrence noted in the malfunction reports were unknown device problem, breakage, overheating and device leak. The most common occurrences in the injury reports were bleeding, thermal burns and foreign body in patient. A specific query for NLQ was not conducted, because adverse events are most commonly entered under the product code of the

original single-use device. A query for the reprocessed version of the single-use devices could be duplicative and result in skewing data inappropriately.

The agency searched the MAUDE database on July 12, 2022, to identify adverse events related to the use of LBK devices. The search was not time-frame restricted and included all MDRs entered into the MDR database by July 12, 2022, that were reported under product code LBK. The search identified 57 relevant MDRs, one death report, 17 injury reports and 39 malfunction reports. The death report was entered into the MDR database in 2012 and, based on the narrative provided, it was not device-related. The most frequently reported patient problems included no impact or consequence to the patient, additional surgical procedure or therapy necessary and hospitalization required. The most frequently reported device problems included unknown device problem, breakage, overheating and device leak.

This slide provides background information for recalls in the medical device recall database. For the sake of time, I will not go through this information in detail since it was summarized previously in the presentation for nail prosthesis under product code MQZ.

The agency conducted a review of the recalls database for ultrasonic surgical devices. The review of the database found 27 recalls for devices cleared under product code LFL. The recalls were related to device design, component integrity, and packaging and sterile barrier integrity. The review found four recalls for devices cleared under product code NLQ. Two of these recalls were related to packaging of the devices, one was related to the lack of a regulatory clearance, and the fourth seemed to be a technical issue. Finally, a review of the database found one recall for devices cleared under product code LBK. This recall is related to an accessory of the CUSA Excel ultrasonic surgical aspirator system that is used for the electrocautery with or

without ultrasonics.

These recalls do not suggest that there are general safety concerns related to the class of ultrasonic surgical devices, but instead, except for the lack of regulatory clearance, are risks that can be mitigated through the proposed special controls. To determine the appropriate classification for ultrasonic surgical devices, we have identified risks associated with these devices and possible mitigations for these risks. We will be asking the panel for input on the list of risks and mitigations. To identify the risks of these devices, we reviewed MDRs, recall information, the literature analysis as previously discussed, and the information available to FDA regarding cleared devices.

Here are five risk categories we've identified for ultrasonic surgical devices: Infection, which can result from devices that are not adequately cleaned or sterilized; Adverse tissue reaction, which can result from use of device materials that are not biocompatible; Bleeding/hemorrhaging/blood loss, which can result from unintended damage to surrounding blood vessels; tissue injury which can be due to excessive energy or heat provided to tissues or mechanical injury due to the power of the device from fragmentation, emulsification and aspiration. Tissue injury can also occur from electric shock resulting from malfunction or failure of the electrical components of the device. Additionally, tissue injury can result in neurological deterioration, prolonged surgical procedure, and death. Finally, interference with other devices: The device emits electromagnetic interference that can affect other surgical equipment used in the procedure or operating room. Also, the device may not have sufficient EM immunity to resist EM interference from other surgical devices in the operating room.

We believe 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 risk to health and provide reasonable assurance of device safety and effectiveness for this device type. The table on this slide shows the identified risks and proposed mitigation measures that will be addressed through special controls.

To mitigate the risk of infection, we recommend sterilization validation, reprocessing validation, pyrogenicity evaluation, shelf-life testing, packaging validation and labeling. To mitigate adverse tissue reaction, we recommend biocompatibility evaluation and shelf-life testing. To mitigate the risk of bleeding, hemorrhaging and blood loss, we recommend non-clinical performance testing, bench testing and animal performance testing. To mitigate the risk of tissue injury, we recommend animal performance testing, non-clinical performance testing, bench testing, device reliability testing, electrical safety testing, software verification, validation and hazard analysis, electromagnetic compatibility or EMC testing, use-life testing, shelf-life testing, and labeling. To mitigate the risk of interference with other devices we recommend EMC testing and labeling.

Here is our proposed classification regulation for ultrasonic surgical devices. Part A of the regulation defines the device as follows: An ultrasonic surgical device is a prescription device intended to heat, fragment, emulsify or remove tissue by use of ultrasonic displacement and vacuum suction. This type of device may include ultrasonic scalpels, ultrasonic vessel sealers, ultrasonic surgical aspirators, and accessories such as assembly tools, wrenches, foot switches and end effector tips. Further we are proposing these be classified as Class II devices with special controls.

Based on the identified risks and recommended mitigation measures, FDA believes that

the following special controls will provide reasonable assurance of safety and effectiveness for ultrasonic surgical devices under product codes LFL, NLQ and LBK.

One, non-clinical performance testing must demonstrate that the device performs as intended under anticipated conditions of use, including the following: A, characterization of the ultrasonic and power parameters, e.g., sonication frequency and displacement, irrigation rate, suction negative pressure. B, bench testing of material strength to demonstrate the device will withstand forces encountered during use and maintain device integrity over the labeled shelf-life and use-life, including repeated cleaning/use cycles if processed.

Two, software used to operate the device hardware must be described in detail in the software requirements specification, or SRS, and software design specification, or SDS. Software verification, validation and hazard analysis must be performed.

Three, electrical safety, thermal safety, mechanical safety and electromagnetic compatibility or EMC testing must be performed.

Four, performance data must demonstrate the sterility of the tissue-contacting components of the device and must evaluate pyrogenicity if intended for neurosurgical use.

Five, performance data must support the shelf-life and use-life of the device by demonstrating continued sterility, package integrity and device functionality over the intended shelf-life and use-life.

Six, the tissue-contacting components of the device must be demonstrated to be biocompatible.

Seven, animal performance data must demonstrate that the device performs as intended

and will not result in unintended tissue injury, including mechanical and thermal damage to surrounding tissue structures.

Eight, the labeling must include, A, qualifications needed for the safe use of the device; B, a detailed summary of the device technical parameters; C, a detailed summary of the device- and procedure-related complications pertinent to use of the device; D, information on how the device operates; E, a shelf-life for sterile components; F, the use-life of the device for reusable components; G, validated methods and instructions for reprocessing of any reusable components; H, information on the electrical safety and electromagnetic compatibility of the device; and I, prominent labeling adjacent to original equipment manufacturer identifying the reprocessor for single use- reprocessed ultrasonic surgical instruments.

This concludes our presentation. Thank you for your time and attention.

Dr. Harris: Thank you. We will now have any clarifying questions from the panel regarding this presentation. Please use the Raise Your Hand function in the Zoom platform. Before we get started, I would be remiss if I did not introduce another panel member who has joined us. Dr. Byron Thompson has joined us. If you would please introduce yourself, your affiliation and area of expertise. Dr. Thompson, are you there? Perhaps he's unavailable. In any case, we'll move on to any – oh, here's Dr. Thompson.

Dr. Harris: Well, when Dr. Thompson gets back, we will have him introduce himself. Okay. So, any clarifying questions regarding the content of that presentation? Seeing none, I have a question for – well, actually, I think I'll save that question. Okay. So, if there are no clarifying questions, I think we can move on to deliberating over the FDA's questions for the

panel. FDA, will you please present the first question.

FDA: We have the following questions for the panel. We are looking for your thoughts and recommendations on the appropriate regulatory classification for these devices.

Question 1. FDA has identified the following risks to health for ultrasonic surgical devices: Infection, adverse tissue reaction, bleeding/hemorrhage/blood loss, tissue injury and interference with other devices. Please comment on whether you agree with inclusion of all the risks in the overall risk assessment of ultrasonic surgical devices under product codes LFL, NLQ and LBK. In addition, please comment on whether you believe that any additional risks should be included in the overall risk assessment of these ultrasonic surgical devices.

Dr. Harris: Thank you. So, this will be an opportunity as a panel to address the risks as outlined by FDA. Specifically, are there risks that we would feel should be removed from that list, or any that should be added? We'll begin with Dr. Baltuch.

Dr. Baltuch: One of the real time risks that always concerns me, and you mentioned in the data, was the ultrasonic aspirator malfunctioning or not working. That was usually due to a variety of issues. But the aspirator would often be hit or miss and have to do with the ability to put it together, to make it work, the heads in general, and that wound up being – you know, not knowing whether it would work that day I thought was the biggest risk over 35 years of doing that.

Dr. Harris: Thank you. Ms. Mary Olivera.

Ms. Olivera: Thank you. I truly believe we can mitigate some of these risks, including the infection risk, by implementing those special controls. Currently these devices are used in critical

procedures, and when they come into the reprocessing area, they're hand-washed, but there's no performance testing being done to these devices. The inspection process doesn't even include utilizing visual aids like borescopes to look inside those channels or the lumens to make sure there's no bioburden inside these devices. It is very important that a performance test is done prior to the sterilization, otherwise these devices go through the sterilization process, which sometimes the device, as it goes through many uses, the life of that device the reduced. So, if there are any issues, it's only found when it gets into the surgical procedure and the surgeon using them.

Dr. Harris: Thank you, Ms. Olivera. I have a clarifying question for you. If I understand you correctly, you think the performance verification should occur prior to the resterilization, and I'm assuming you don't think the resterilization process itself could alter the performance behavior of the device?

Ms. Olivera: So, every device that we sterilize, we should test prior to putting it through the sterilizer. The chances of that device malfunctioning during the procedure because of the sterilization process, they're minimized if we test those devices before we use them. We do that for other instrumentation. We test bipolar forceps used during laparoscopic procedures. So, there should be some test that can be performed prior to the packaging of that device.

Dr. Harris: And one of the questions, sorry, for you, do you believe there should be any specifications regarding how these devices are resterilized in terms of the methodology, whether this is gas or, I don't know if we even use ethylene oxide anymore, but what are the options, and should that be specified?

Ms. Olivera: Certainly, some of the IFUs' instructions for use do include specifications in terms of pressure, temperature, and drying time. And it should be very clear, what are those processes? We utilize different modalities from steam to low-temperature sterilization. Yes, a lot of the hospitals nowadays do not have ethylene oxide, or we've moved to a much friendlier process using hydrogen peroxide sterilization. So, yes, clear instructions that can be validated at the factory, but also can be duplicated at the hospital setting, are very, very important in our field of work.

Dr. Harris: Thank you. Dr. Tjoumakaris?

Dr. Tjoumakaris: I want to make sure, in the adverse events slide, I did not see mortality listed there and I know certainly by experience of seeing these devices used in the hospital and also based on the research that is presented, there is a risk of mortality, sometimes operator dependent, sometimes device malfunctioning dependent. Is that something we should include in the adverse events?

Dr. Harris: As a panel member, they're actually looking for your advice and recommendations, so if that's something you feel should be added, then that should be noted by the FDA.

Dr. Tjoumakaris: Thank you.

Dr. Chen: Is it okay for us to comment on some of the questions brought up by the panel at this time?

Dr. Harris: Absolutely.

Dr. Chen: Because talking about the mortality, I mean, those information, I thought it was

included in our adverse event summary. And certainly, when we do that, we certainly would ask the sponsor to include the information, the relevant information in the labeling in the future. And going back to the sterilization related issue brought up earlier, I do want to clarify that, when we're talking about reprocessed devices, for us, yes, we do make sure that the device is going through the reprocessing so-called procedure clearly. And after the reprocessing, the way we evaluate the device for the reprocessing device, we evaluate the performance testing after the device has been reprocessed. So, we do that, also. And I don't know whether that clarified the concern that you just raised.

Dr. Harris: No; very much, very much. Dr. Cormier?

Dr. Cormier: I would echo the comments regarding the mechanics of those as operators. You know, it's very difficult to say that just because you tested once after the sterilization process that it's going to function appropriately throughout the entire procedure. We've had issues with again the setup, whether or not the numbers that you see on the settings are actually what you see in real time. The handles can heat up, and so there can be some mechanical issues that create some – burdensome to the surgeon.

However, I would want to know if the workup prior to any sort of resection was appropriate. If there is a relatively good geographical outline of the vasculature and the other surroundings as the clinician approached that specific tumor. But again, the mechanics of that device as you're using it, we have seen a number of breakdowns. So, the mortality issue that was brought up a few seconds ago, I think that should be added to the risks.

Dr. Harris: Okay; thank you very much.

Dr. Chen: Dr. Harris, can I make comments?

Dr. Harris: Absolutely, Dr. Chen.

Dr. Chen: This is Long Chen. Regarding our testing, we do have one item is for the so-called non-critical performance testing, and in that performance testing, we do ask the sponsor to test the device mechanically and also for the thermal effects. And we can only do so much to ensure that the device will function the way it's supposed to be. But certainly, I mean, we all understand, there's a certain so-called – still have certain possibilities that the device may not function the way it was designed for.

Dr. Cormier: Can I comment on that?

Dr. Chen: Yes.

Dr. Cormier: I guess what I'm saying is, if you're using that device for 30 minutes versus perhaps two or three hours, there might be some safeguards with regards to that. So, as you use it, it may be more likely that it's going to heat up and failure issues may come into play once you breach a certain time limit. Perhaps that should be considered, perhaps that might have added to the mortality, even what we see in terms of what was mentioned earlier with the posterior fossa syndrome. A lot of this depends on the technician itself, but the mechanics of those devices are again – certainly play a big part in this as well.

Dr. Harris: I just want to remind the panel that what I'd like to focus the remainder of this discussion is on this question, which is simply asking our thoughts around what risks should be listed or perhaps removed from the proposed list. We will then spend time delving into the actual recommended mitigations or special controls where some of these comments will again need to

be, I think, considered.

So, are there any other risks that people would like to either add? We've heard comments about adding death as a risk. Or any of the risks that were listed that you think should be removed? Dr. DeLong.

Dr. DeLong: I have a question I guess for the neurosurgeons on the panel. Is there ever an issue with these devices, multiple moving parts where pieces might fracture off or break off. Has that ever happened? Is that a realistic risk or just me making stuff up?

Dr. Harris: Any questions for our neurosurgeon? I'd like to take a moment to introduce Dr. Byron Thompson who has joined us. Dr. Thompson, if you could tell us a little bit about your affiliation, your position, and your area of expertise.

Dr. Thompson: I'm a neurosurgeon at the University of Michigan. My expertise is in vascular and skull-based surgery. And I apologize for the delay. I know I signed on early, but I thought I was supposed to be here at 11:00 a.m. until I got the message, so I apologize.

Dr. Harris: No problem. So, would any of our neurosurgery panel members like to address Dr. DeLong's question regarding fracture or fragments of these devices perhaps becoming detached during surgical procedures? Dr. Baltuch.

Dr. Baltuch: Yeah, that would happen not infrequently, in the reprocessing, it's not infrequent that these aspirators come back defective from reprocessing, and you have to push to get a new head and new device. So mechanical problems and breakage and all these things remain an enormous issue with the device. That being said, this device was a total game-changer in neurosurgical care, for me, after about 40 years of this use, 40 to 50 years, it has changed the

way neurosurgery was done and I think it has spread to other specialties. But yes, there was breakage.

Dr. Harris: Any other comments regarding this issue of device breakage? I believe that that risk – well, let me ask the FDA, do they feel that that risk is in fact included within the list that was proposed?

Dr. Chen: This is Long Chen. Yes, I mean from MDR, actually, we have observed a lot of MDRs related to the device fracture. And for device malfunction, certainly, those are part of the risks that are included in our list.

Dr. Harris: Thank you, perfect. Dr. Bryant?

Dr. Bryant: And thanks for that clarification, Dr. Chen. That's kind of where I was going. Dr. Baltuch, specifically around the breakage. Can you articulate that again? You were mentioning after the reprocessing – I just wanted to make sure I heard you clearly, what you're referring to there.

Dr. Baltuch: Classically there were a variety of things. You'd get, the heads would become – the aspirator; the plastic or the metal piece would become – would change in their position after reprocessing, changing the positioning. That would potentially change the entire functioning of the device. You'd get breakage into the plastic, things going in that were irrigating the entire system, those would also break. It was interesting, it was not totally uncommon coming back from sterilization to have bits of bio-material from previous cases that you would identify on the cases as you took it out, that happened more often than we'd like to comment. Again, a device that's fabulous when it's working and a game-changer to neurosurgery, but a

device most neurosurgeons know they need to have plan B in place when that device is not operating.

Dr. Harris: Thank you. Dr. Galandiuk.

Dr. Galandiuk: It sounds according to Dr. DeLong's comment and Dr. Baltuch, according to your comment, that some kind of risk or comment should be added to this, but not being a neurosurgeon, I don't know how that actually affects the case. I assume that adds time or at least annoyance on the part of a neurosurgeon when that happens, that it prolongs the case. Does that risk tissue injury, or adverse outcome intraoperatively when something like that happens? Or how should that – does that have to be added as an increased risk or added operative time or device failure? How would you incorporate that as a risk in this list?

Dr. Harris: Any suggestions, Dr. Baltuch, or any of our other panel members. Any concern over how that concern and/or fracturing and/or biomaterial, residual biomaterials on that device, how that can be adequately captured in the special controls being suggested.

Dr. Baltuch: I don't know if they can put something in about performance in the device, that it should demonstrate performance and repeated performance?

Dr. Harris: Dr. Chen, can you comment on that?

Dr. Chen: Yes, thank you for those comments. Yes, in the non-clinical performance testing that we evaluate, we do look into the reliability test for the device. And we certainly want the sponsor to demonstrate that the device would be reliable in usage. So that's what we ask. We include that in the testing requirement.

Dr. Harris: Dr. DeLong?

Dr. DeLong: I guess, in light of Dr. Chen's clarification, it does seem like my question is pretty well housed within device malfunction because that's such a general and broad term. Really, I guess what I was getting at was, from my limited time in general surgery, sometimes with laparoscopic procedures, we have the jaws of the device fracture off. You have to try and fish it out in the laparoscopic case, and it seems like there's a risk for retained material or retained fragment. I don't know if that's a realistic risk in neurosurgery since it's not a large cavity like the abdomen or anything. But again, it seems like this is all housed – it's mechanical stability within the device dysfunction risk.

Dr. Harris: I think we can be thinking about, as we move forward, to interrogate the special controls themselves, which will be our upcoming question, how we might want to suggest those sorts of risks or malfunctions be tested for or mitigated. Ms. Agazie?

Ms. Agazie: Ms. Agazie here. I guess I have the same question. How do we ensure ongoing non-clinical performance testing throughout the whole identified risk? Ongoing, non-clinical performance testing, with that device.

Dr. Harris: Once again, I think that's something we'll be discussing or should discuss in the next question. I think that will fall under this rubric of device malfunction. So maybe we'll just table that for a quick few moments. I was wondering whether or not, why the risk for pyrogenicity was specific to the neurosurgical devices and not for the entire category of devices? Can anyone from FDA or our expert, Dr. Zheng, could comment on that?

Dr. Chen: Dr. Harris, can I have your question again?

Dr. Harris: Sure. In the list of risk mitigations – or proposed risks, rather, there was a

specification of testing for pyrogenicity, but it qualifies only for the instruments used for neurosurgical indications and I was wondering why pyrogenicity concerns wouldn't be applied to all of these ultrasonic tools. I certainly would be concerned about using an instrument in the abdomen that was potentially pyrogenic.

Dr. Chen: Can I ask Dr. Zheng to comment on that?

Dr. Zheng: Yes, this is Dr. Zheng. I'm the Division Director for Division 5A for Neurosurgical, Neurointerventional and Neurodiagnostic devices. I think that's a great question. We did believe that the pyrogenicity risk is especially concerning in the brain because of the risk for bacterial endotoxins from the device, and especially since these devices are reprocessed. If the panelists believe that that's also a risk for general surgical use, that is definitely something that we can incorporate into the risk and risk mitigation table, to include pyrogenicity evaluation for all potential uses of these devices. So, thanks for that recommendation.

Dr. Harris: Sure. Any other comments regarding just the list of risks associated with these devices? If not, then I think that will summarize the comments from the panel regarding the list of risks for this class of devices --

Dr. Cormier: Sorry.

Dr. Harris: Who is speaking?

Dr. Cormier: This is Jason Cormier. You might have mentioned this already, but going back to the fragmentation of the breakage issue, should we not add that as a potential, retained fragments as part of the risk, or is that something we'll discuss perhaps in the next section?

Dr. Harris: I think that we'll – I was thinking that that would be something we can talk

about under the actual special controls, the category of device malfunction was fracturing and breakage. But if FDA can see that that needs to be specifically added to the list of specific risks, then please note that comment at this time.

Dr. Krause: This is David Krause. We think that panelists should mention any risk that they feel is valid, and we consider those risks, and we look through them, and we look at our list of risks that we have put together, and if it fits in one category, maybe we might expand that category a little bit so that that risk is included, or we may add that risk as a separate risk. So, I think any risk that anyone on the panel feels is a legitimate risk should be mentioned, and we'll be happy to consider it.

Dr. Harris: Thank you. Are there any other risks that any panel members would like to discuss? Dr. McGrath?

Dr. McGrath: Sorry, I can't get my hand raise to work. I have a question for general surgeons using these devices. Is there any – it's mentioned in some of the literature. Is there damage to other organs other than the thing that you're specifically working on with the device in the abdomen? Because again, I agree with the way the conversation has been going that this is a bit neurosurgical centric, but perhaps under the tissue injury where it mentions neurologic deterioration, should it also call out damage to adjacent tissue in the abdomen or other questions in the body? I guess a question for you, Hobart.

Dr. Harris: I think that's a great question. I think there can be obviously thermal spread adjacent to the areas where we're operating, but what I've also seen is where there can be – and I'm not an expert in this area – but the instrument can apparently short or there can be areas

where tissues that are actually sometimes even out of the line of sight of the surgeon performing laparoscopic procedures, for example, there can be issues with electricity being transmitted from other breaks or areas that are improperly insulated. So, I think that is a concern, but I was thinking that would fall again under this context of electromechanical dysfunction. But I think that is worth pointing out to FDA that that sort of injury, I've certainly seen that occur. Remember to give your name for the transcriptionist. Dr. Baltuch.

Dr. Baltuch: Historically, when the [indiscernible] came out for use in our surgery, it didn't have a coagulator associated with it, it was purely ultrasonic aspiration with no heat at all. Then probably about 20 or 25 years ago – one day all of a sudden, they came up and put a coagulator on it. Where we previously used bipolar coagulation in the brain, all of a sudden you have the equivalent of a coagulation which would look like monopolar co-ag, which we never used in neurosurgery in the brain historically. It's exactly as described. It was a ton of heat coming up and I disconnected it immediately when I saw what it looked like and never used that coagulator again. Now, I think if you speak to younger neurosurgeons who do a lot of tumor work or skull-based work, they probably use it quite effectively. But in the beginning, it looked really – it was scary.

Dr. Harris: Any other comments? So, then Dr. Krause, is that sufficient feedback from the panel on this question?

Dr. Krause: This is Dr. Krause. I think, yes, I think the discussion has been excellent and thank you for all the suggestions.

Dr. Harris: Thank you. So, FDA, can you please move on to the next question.

FDA: Question 2. Section 513 of the Food, Drug and Cosmetic Act states a device should be Class III if sufficient information exists to determine that general and special controls are sufficient to provide reasonable assurance of its safety and effectiveness, and if the device is purported or represented to be for use in supporting and sustaining human life or for a use which is of substantial importance in preventing impairment of human health, or if the device presents potential unreasonable risk of injury or illness.

A device should be Class II if general controls by themselves are insufficient to provide reasonable assurance of 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 recently 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 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 does not present potential unreasonable risk 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 reasonable assurance of device safety and effectiveness for this device type. As such, FDA believes that class II is the appropriate classification for ultrasonic surgical devices under products codes LFL, NLQ and LBK. Following is a risk mitigation table, which outlines and identified risks to health for this

device type and the recommended controls to mitigate the identified risks.

The identified risks to health include infection, which can be mitigated by sterilization validation, reprocessing validation, pyrogenicity validation for neurosurgical devices only. Shelf-life testing, packaging validation and labeling. Adverse tissue reaction, which can be mitigated by biocompatibility evaluation and shelf-life testing. Bleeding, hemorrhaging and blood loss, which can be mitigated by non-clinical performance testing, bench testing, and animal performance testing. Tissue injury, which can be mitigated by labeling, non-clinical performance testing, bench testing, device reliability testing, electrical safety testing, electromagnetic compatibility testing, software verification, validation, and hazard analysis, animal testing, shelf-life testing, and use-life testing. Finally, interference with other devices, which can be mitigated by electromagnetic compatibility, testing and labeling. Please discuss whether the identified special controls for ultrasonic surgical devices appropriately mitigate the identified risks to health and whether additional or different special controls are recommended.

The proposed special controls are as follows.

1. Non-clinical performance testing must demonstrate that device performs as intended under anticipated conditions of use, including the following. A: characterization of the ultrasonic and power parameters e.g., sonication frequency, and displacement, irrigation rate, suction negative pressure. B: Bench testing of material strength to determine the device will withstand forces encountered during use and maintain device integrity over the labeled shelf-life and use-life, including repeated cleaning/use cycles if reprocessed.

2. Software you used to operate the device hard washing must be described in detail in

the software requirements specifications or SRS, and software design specification, or SDS. Software verification validation and hazard analysis must be performed.

3. Electrical safety, thermal safety, mechanical safety, and electromagnetic compatibility or EMC testing must be performed.

4. Performance data must demonstrate the sterility of tissue contacting components of the device and must evaluate pyrogenicity if intended for neurosurgical use.

5. Performance data must support the shelf-life and use-life of the device by demonstrating continued sterility package integrity and device functionality over the identified shelf-life and use-life.

6. The tissue contacting components of the device must be demonstrated to be biocompatible.

7. Animal performance data must demonstrate that the device forms as intended and will not result in unintended tissue injury including mechanical and thermal damage to surrounding tissue structures.

8. The labeling must include: A. Qualifications needed for the safe use of the device. B. A detailed summary of the device technical parameters. C. A detailed summary of the device and procedure-related complications pertinent to the use of the device. D. Information on how the device operates. E. A shelf-life for sterile components. F. The use-life of the device for reusable components. G. Validated methods and instructions for reprocessing of any reusable components. H. Information on the electrical safety and electromagnetic compatibility of the device and I. Prominent labeling adjacent to original equipment manufacturer identifying the

reprocessor for single-use reprocessed ultrasonic in surgical instruments

Dr. Harris: Thank you. So now I would like our panel to deliberate the – really the question of, are the special controls adequate to mitigate concerns regarding risk and effectiveness of these ultrasonic instruments? Once again, we won't be talking so much about the nitty gritty of the mitigation measures, but just do we feel special controls of this nature are sufficient in and of itself to mitigate these risks and thus be consistent with mitigating these devices as Class II. Any comments from the panel? Dr. Li.

Dr. Li: I hope this not too much in the nitty gritty, but when you are talking about the validating use-life or shelf-life, does that include the number of times the device has been reprocessed, and does it include the amount of time the unit was used? I think Dr. Cormier said the use time of the device time could be from minutes to hours. Is there a restriction or some tracking of how many hours a device is used and how many times it is been resterilized and are there limits to either one of those?

Dr. Harris: Thank you. Do we have a response from someone at the FDA?

Dr. Chen: Yes. To answer the question, yes, we do from the shelf-life versus the use-life test.

Dr. Harris: Dr. Chen, I'm having a hard time hearing you, I don’t know if other panelists are as well – either turn your mic up or get closer to your mic.

Dr. Chen. I will do that.

Dr. Harris: Can you try speaking now so we can hear you?

Dr. Chen: Yes. We do include that in our testing.

Dr. Harris: Dr. Chen if you speak up a little louder because it is fading out.

Dr. Chen: I don't know if you can chime in, Dr. Zheng, if you can chime in and see if you can help?

Dr. Zheng: Hi, can everybody hear me?

Dr. Harris: Yes.

Dr. Zheng: I can help try to answer this question. For shelf-life, we typically validate the shelf-life for sterile components if they are already provided presterilized because we want to be sure the devices are stable and are sterile before using. And the shelf-life is typically validated for sterile components.

The use-life is typically validated for the reprocessed device components, and we look at the worst case. So, we look at the expected number of times the device would be reprocessed during it is expected clinical use-life. And then we also look at how many times the device would be in operation, including the duration of surgery, and if it is reusable, it may be the number of surgeries or the duration it will be used. So that is typically how we look at validation of this device use-life. Does that help answer your question, Dr. Li?

Dr. Li: Yes. A quick follow-up. My concern, material is one that I am worried about. That with multiple sterilizations or long hours of use that there will actually be degradation or change of the material over time that you don't intend.

Dr. Zhang: Yeah. Sure. Definitely. And that's something that our reviewers take a look at

as far as use live evaluation. We may look at different parameters, how the device performs after the use life. It could include a visual or microscopic evaluation of the device material. That's great suggestion, and we'll take that back.

Dr. Harris: Ms. Mary Olivera.

Ms. Olivera: Hi. So, in those validated instructions for reprocessing, will the tools required or needed to ensure that the device is cleaned properly be included – like lumens, or any bioburden, and one of the things we should be looking for in terms of inspecting this device prior to packaging and sterilization, so we can ensure at least the device is ready for use in proper condition functionality.

Dr. Harris: Thank you. Dr. Galandiuk.

Dr. Galandiuk: I was wondering, when we are talking about the animal use on that, I would there wouldn't be a lot of difference in terms of the impedance of tissue depending on the type of animal was selected and how relevant that would be to human use and that would depend on if they are doing homeostasis or different things and I would be interested in any comments on that.

Dr. Harris: Dr. Zheng, Dr. Chen, Dr. Krause?

Dr. Zheng: I can help answer that question. I will ask for feedback from my other colleagues as well. When we look at the animal models for device safety and performance, we do look at the relevance of the animal model for intended clinical use. We look at what types of tissues the device might be targeting and we try and model that in the animal model making sure it is as clinically relevant as possible. We take that into consideration with the animal study

design. Dr. Krause, Dr. Chen, do you have anything to add?

Dr. Krause: I agree with what you just said. If the instrument is intended to be used in the liver, we look for the animal that is the best complement to the human. We might use a large porcupine model or something like that. Your statement is exactly what we do. Thank you.

Dr. Harris: Dr. Cormier. You are on mute.

Dr. Cormier: Apologies. I wanted to piggyback what Dr. Li brought up again, thank you for bringing that up. In regard to something like spinal surgery when they evaluate instrumentation, they look at the number of revolutions and getting back to the point, the time [indiscernible] that you utilize the instrument in the operating room to try to predict failure. I really haven't heard anything as to some sort of time duration. Should you be more cautious after utilizing it for 45 minutes or two hours?

I think that – I haven't heard – maybe I missed it, but I haven't heard an explanation as to how you might track that, and it be entered in this special condition.

Dr. Harris: Excellent. Dr. Bloom?

Dr. Bloom: It's a follow-up on Dr. Cormier's point. Certainly, I have been handed a harmonic scalpel fresh out of the box that failed its calibration before I used it on the patient. That speaks to the strength of the software, finding a problem with the device. If we put limits on the amount of time a particular device is activated or number of cycles reprocessing, should that also be built in the software of the – not the hand-held unit, but the wall unit for lack of a better term to provide additional protection?

Dr. Harris: Very good. Dr. McGrath?

Dr. McGrath: I would like more information on item 8-C. It says a detailed summary of procedure-related complications pertinent to use of the device. Does that mean that for every different procedure, which you mentioned during the presentation, are very numerous, that would have to be provided for – the list would have to be provided for every one of those? Is that the intent for that particular labeling requirement?

Dr. Davis: Thank you. Someone from FDA. Dr. Chen, Dr. Krause –

Dr. Chen: In general, that's correct.

Dr. Harris: That's a yes.

Dr. Chen: Yes, that's correct. Can I go back to Dr. Li's question?

Dr. Harris: Absolutely.

Dr. Chen: Regarding the use-life, I want to bring this to your attention. In our review of the performance testing data, what we ask sponsor to do is provide the worst-case scenario of performance testing information. It is up to the sponsor to define, what is the longest time the device will be used. And then based on that, as a worst case, to provide the performance testing information. In our mind, we hope by asking that, that would cover the use-life related concern that was brough up by you.

Dr. Harris: If I understood Dr. Bloom's comment, and correct me, Dr. Bloom, if I am misstating you. The question is whether or not there might be an opportunity for not only a manual measure of the performance of the instrument, but a software measurement, or a software guide. Because I don't know whether the devices can be tracked individually, but – is that what you are referring to, Dr. Bloom?

Dr. Bloom. I don't know, but I think every handheld, the modern handheld devices have unique identifiers from the software portion, so I think the particular device can be tracked through its lifespan – use span.

Dr. Harris: Dr. Cormier, your hand is still up. Do you have another comment for us?

Dr. Cormier: No, I'm sorry.

Dr. Harris: No problem, I can lower it for you, taken care of. Any other comments? Dr. Li.

Dr. Li: I don't want to beat a dead horse here, but I think to Dr. Chen's comment about the worst case, it seems like these are very complicated devices that are reusable. There are mechanical connections, there's multiple polymeric and metal materials, there's cavities and then there are all sorts of electronic components that are exposed to multiple cycles of some kind of sterilization process, hydrogen peroxide perhaps, and also, they are used for different lengths of time. I'm not sure the worst-case scenario is. It seems the worst-case scenario would be one device that was used 20 times for hours at a time and sterilized 10 times and then you get into a problem. If you just take one use and one sterilization cycle, that really to me is not a worst-case scenario.

Dr. Harris: To dovetail on Dr. Li's comments, it sounds as though, and maybe the FDA is already planning this, but the issues of use-life will be more granular-specific in terms of either hours, revolutions, number of times they can be reprocessed, et cetera. And that seems to me to be really strongly held feeling of the panel.

Dr. Chen: Let me follow-up on the comments again. Thank you, Dr. Li, for your

comments, however, I do want to point out that the majority of those devices, they are designed for single use, okay.

And only those that has been reprocessed, which is the NLQ product code, that is reused. And for reuse device, we have different ways of testing and different so called performance testing requirements for that reprocessed device, and hopefully, and that clarify your concern. Majority of devices as we understand they were designed for single using device. Okay.

Only those that have been reprocessed by reprocess manufacturers fit into that NLQ product code as a reprocessed, single-use device. For us, we put it in separate category because we have additional requirements to verify their reprocessing process, and also the performance of the reprocess device still matters and that's the reason for those devices to be put under the NLQ product code.

Dr. Harris: Dr. Delong?

Dr. DeLong: I have a more specific question to address Dr. Li's comment. Do you inform the labeling based on the performance testing? Is that how it works? So, if the manufacturer shows it can work four hours without a problem after the third sterilization, then it would be clearly printed in the labeling, cannot be re-sterilized more than three times, or use not to exceed four hours or something like that. So, you know whatever source they pick is then what they are allowed to put on the labeling, so the users are aware that that was the worst case that's been tested.

Dr. Harris: Dr. Zheng.

Dr. Chen: This is Long Chen. Yes, for us to review the labeling – the worst information

– yes, I mean that should be disclosed in the labeling, that's correct. And for reprocessed device it's always being put in the labeling how many times the device has been used and how many times this device can be reused for the reprocess device.

Dr. Harris: Thank you. Dr. Galandiuk.

Dr. Galandiuk: Dr. Chen, I am a little bit confused when you say a reprocessed single-use device, does that mean hospitals are reprocessing single-use devices to save money for things that should not be done? I am not clear about that.

Dr. Chen: Let me clarify that for you. Some of the devices are designed for multiple use. And for multiple use devices, the healthcare facility has instruction for use, how you can re-sterilize those devices. That is one category, that's what we call the multiple use device category. However, what we are talking about here, the LFL or LBK product code devices they are single use devices. Single use device is only used once and then is disposed. Some of the manufactures recover those disposed, so called single-use device and reprocess it. That's what we call the reprocessed single-use device and that is the reason we put it under the NLQ product code. And it is a totally separate device the way we look at it because of all of the concerns that have been raised by all of you.

We have a very detailed process requirements they need to go through for a reprocessed device.

Dr. Harris: I have a question. And this kind of dovetails on a comment from Dr. Bloom earlier, having the experience of opening an instrument and it not working. I'm curious when manufacturers are producing these devices, are they required to test every device? Or do they do

some sort of sampling of every fifth or tenth device? Does FDA know – because it would seem to me when you have a device that really needs to perform with one hundred percent, as best you can guarantee that perhaps every device should be tested before it's sold. Anyone from FDA can address that?

Dr. Chen: I don't think we have the requirements for them to test every single device before they are shipping that or putting that on the market. We do have a sampling, a measure to test those devices to ensure that the quality is within the specification for manufacturing those instruments or devices.

Dr. Harris: I don't know if anyone on the panel has manufacturing expertise, but it would seem to me that would be a relatively low bar for a manufacturer of an instrument that's going to be used in neurosurgery or the abdomen to guarantee that each device has been tested. You wouldn't buy a car that hadn't been tested, or a watch without it being tested. Why these devices would not all be tested, that would certainly be my suggestion. Dr. Galandiuk?

Dr. Galandiuk: Are these reprocessed sold or marketed as reprocessed devices, or marketed as such?

Dr. Chen: Exactly, we differentiate that very much. For the reprocessed single-use device the label should have a very specific label indicating that this is reused, reprocessed, single-use device. That's correct.

Dr. Harris: So, to summarize, I think the committee feels that, and of course, correct me if this does not capture your opinion, that the – this is a class of devices that the risk of safety and efficacy or effectiveness can be mitigated with special controls. You have heard numerous

comments regarding specific aspects of those controls with a lot of focus on ensuring that the use-life is aggressively or rigorously tested and documented in the instructions for use. Dr. Chen, you have a comment?

Dr. Chen: Yes, thank you for all of the feedback. We would ensure in the future that those –

Dr. Harris: Unfortunately, your audio is going in and out again.

Dr. Chen: I want to say, yes. Thank you for the comments and we certainly want to ensure that in the future, the labeling information would have that information you recommended.

Dr. Harris: Dr. Li, you have a comment?

Dr. Li: Yes, about the manufacturer's perspective. I used to be an owner of an orthopedic manufacturing company. From what the neurosurgeons said, Dr. Baltuch said, you go into it with a plan B, because you have to be ready for the device not to work. And Dr. Harris you said that this is such an important instrument and have to have it dependable. I would say that it’s not so much that the controls are not in place, but I would say the controls, the way – perhaps the details of controls are not adequate when the neurosurgeons always have to go in with a plan B. If they are not testing every device, that would be problematic. So, the results in the MAUDE reports basically, I would say the malfunction rate is higher than I would really like it to be.

It doesn't really have so much to do with whether or not it is on your mitigation list or whether or not you are looking at those things, but whatever controls you’ve got now, I hope could be improved.

Dr. Harris: Thank you. Any other final comments? Dr. Krause, is this feedback sufficient?

Dr. Krause: Thank you. Yes.

Dr. Harris: We have another comment from Dr. Galandiuk.

Dr. Galandiuk: I was wondering from the FDA what percentage of ultrasonic equipment like this, so they estimate is constituted by the reprocessed equipment overall?

Dr. Chen: I do not have that kind of information, not with anyone from our team has that kind of – [Indiscernible].

Dr. Harris: Your audio is again cycling.

Dr. Chen: Sorry about that. I don't have that information. I don't know whether our team members have this kind of information.

Dr. Harris: Unfortunately, we can't hear you. It sounds like he doesn’t have that information.

Dr. Chen: Yeah. I don't know this kind of information and I do not have that, yes.

Dr. Harris: Ms. Agazie.

Ms. Agazie: I just want better clarification, is the panel suggesting that we add more mitigation measures to reprocessed devices, or just the new devices. I just wanted to clarify.

Dr. Harris: My impression of the discussion is that the overall categories of risk mitigations are acceptable to the committee, but there has been a lot of focus discussion on the

need to be quite specific and granular when it comes to the life cycle of the instruments, and that it be adequately reflected whether it be in the labeling but that certain specifications, pyrogenicity, or post manufacturing testing would apply to all of the devices and not specifically the reprocessed ones. I don't know if anyone else had other comments they wanted to make sure are adequately emphasized or captured by the FDA. Dr. Krause if this is sufficient, move on to the next question. FDA, would you please read that for the panel?

FDA: Question 3. Please discuss whether you agree with FDA's proposed classification of Class II with special controls for ultrasonic surgical devices under product codes LFL, NLQ and LBK. If you do not agree with FDA's proposed classification, please provide your rationale for recommending a different classification.

Dr. Harris: Okay, the question for us now is are we comfortable, do we feel we can support this proposal that these devices be regulated as Class II devices with special controls and now would be the time to ensure that any thoughts you have regarding the specificity and content of those special controls be shared with the FDA. Comments from the panel? Dr. Baltuch.

Dr. Baltuch: Just a question. Two questions. So, if this was a Class III device, just for clarification, as opposed to a Class II device, what would that entail in addition to bringing a newer device to market?

Dr. Krause: So, if these were classified into Class III, there would be a time period where the FDA would put out a Federal Register notice saying we're moving these devices to class III. And then there would be a period of time, and those periods of time are not specified, but I think the minimum would be three months or six months between the announcements, but it could be

longer. For some, it's been a very long time. But then, every manufacturer that is currently on the market, if they want it stay on the market would need to submit a PMA, which was discussed earlier, the premarket application. If they did submit a PMA, their product could stay on the market while their PMA was being reviewed.

If, however, FDA decided the PMA doesn't have sufficient information. That product would go off the market. If at the time that PMAs are called for, the PMA is not submitted, that company's product would go off the market. The amount of information might include clinical data, it might include all of the testing that you have seen, approved PMA's require annual reporting, where the company is required to provide an annual report every year.

They also have much more stringent rules for manufacturing. Every small change in manufacturing needs to be submitted to the FDA. Does that answer your question?

Dr. Baltuch: Yes. So, my follow-up question to that, if you have – with the class II. Would class II prevent them from developing sort of a Walmart version of an ultrasonic aspirator which then got thrust upon neurosurgeons in this country by hospital systems looking to cut costs? That is the de facto of what happens to us in real world time.

Dr. Krause: Keeping these at Class II, there are requirements for review, if it meets those requirements, it goes on the market. If it does not meet those requirements, it will not make it to the market. So, if a Walmart version, as you so described it, checked all of the boxes that we review, it could get on the market because it met the requirements of previous devices of the same type that we had seen before and met those same parameters and same endpoints, et cetera. If it didn't meet those endpoints, we would not need it on the market, and it would not be

something that would get cleared.

And our review staff are very thorough in how they do their reviews and I would trust that they would catch any version of the device that is not fully, you know – meet the endpoints we have set for those devices.

Dr. Chen: This is Long Chen. I want to mention that all of the devices we create are for prescription use only. And if it is going to be for Walmart. The general, OTC use, that would be a different intended use, and certainly it is not going to be included in what we discuss here today.

Dr. Harris: I think Dr. Baltuch's comment, and I can endorse that comment that you do see devices I'm sure are meeting the mechanical and benchtop testing requirements, but when you actually operate the instrument, it appears to be much less – its structural integrity is diminished and materials seem to be visibly less expensive to manufacture, at least that's how it strikes one. So, I think it would seem to me, if the special controls are sufficiently rigorous, hopefully it will not be cheap alternatives that can meet that testing requirement yet perform at a less than desirable level. Dr. Li.

Dr. Li: Yes, Steve Li, a clarification question. If I understand the data presented, that there were – death is obviously a very significant adverse event that we have listed, and there seem to be some indication that there were some device failures related to the cause of death, is that correct? Are there some device failures that have been identified as being the cause of mortality?

Dr. Harris: Dr. Zheng, can you or one of the content experts address that question? You

are on mute, Dr. Zheng.

Dr. Zheng: Sorry. I believe based on our Literature review, we have been able to identify that there were some deaths that were related to the device. And then some of the deaths were related to potentially the disease, but yes, there were some related to the device, at least based on our literature review and the MDRs we received.

Dr. Bryant: Dr. Harris, can we look at that information again? That generalization I think – because this is a general critical question, some versus some, I think we need to see the actual data, so the panel understands what attributed to and not. We are talking tens of millions of use cases and it is important to look at that data versus generalizing so and we can answer Dr. Li's question, we need to be specific here, this is critical.

Dr. Li: The follow-up question to that is, if there are device related mortalities, do we know enough about what – with the special controls that you propose in class II. Would they mitigate the chance of those deaths occurring in the future?

Dr. Harris: Right. So, do we have the capability of going back to the presentation and showing us the slide that addressed the data derived from the literature review around deaths associated with this class of instrument?

Dr. Chen: Dr. Harris, can I check with my team and see if it is possible for us to go to the MDR information we summarized?

Dr. Harris: By all means, we'll do that and hopefully get back to that question. In the meantime, Dr. Cormier, you have you your hand up?

Dr. Cormier: Yes, thank you. I think I'm comfortable with the current classifications, like

you said, as long as some of the special controls are mitigated. This is expensive instrumentation, and I would like to know specifically – which I don't think it will be a difficult task for the companies to do, tell us, give us some guidelines as to the duration of time during surgery. And to the comments made about mortality, if you are doing an olfactory meningioma and you have the arteries wrapped up in that tumor and this thing fails on you, you get into an artery and that's a stroke and/or death. [indiscernible] meningioma and it's the same thing. And you get the same thing, you get into some very important neurovascular structures and if you're getting towards a time on it – at least it becomes more predictable and there are some safeguards placed into the software, that you can at least mitigate some of the risks as you are operating, and you can maybe switch handles or what have you. I would be comfortable with it as long as some of those things were truly integrated and into the safety measures. It is not a very forgiving atmosphere when you're in the brain on very important vascular structures.

Dr. Harris: Understood. Dr. Galandiuk.

Dr. Galandiuk: I have the report that you sent out, if you want, I can read about the deaths. Or you can wait until they find it from their information.

Dr. Harris: Well, I think reading it, and we may see it a second time, go ahead.

Dr. Galandiuk: It is on page fourteen on the 36-page report, and it says: "Of the 56 deaths reported, 34 did not implicate the device in the death of the patient and 9 were initiated from literature, and 13 were identified as potentially related to use from the device. Data was extracted from the 13 death reports that implicated the device in the deaths the patients. One case during a liver dissection uncontrolled bleeding occurred after using the harmonic scalpel to

dissect tissue and the patient died intraoperatively. The remaining 12 event narratives detailed that at the time of surgery, the device appeared to seal and cut the tissues and vessels without incidents. The patients were closed and transferred to the intensive care unit or post anesthesia care unit. Postoperative vital signs began showing signs of distress and potential internal bleeding. The remaining 12 event narratives detailed that at the time of surgery, the device appeared to seal and cut the tissues and vessels without incidents. The patients were closed and transferred to the intensive care unit or post anesthesia care unit. Postoperative vital signs began showing signs of distress and potential internal bleeding. The patients were taken back to the operating room for exploration and found to have bleeding from the site of dissection where the harmonic scalpel was utilized. In one case, an unidentified vessel of the neck that had been sealed and cut with a harmonic scalpel had reopened causing of massive bleeding that led to patient death. The event narratives from two reports, detailed bleeding from mesenteric vessels where the harmonic scalpel was used to seal and dissect tissue. The remaining nine event narratives, all detailed dissection of gastric vessels that appeared to be sealed and dry during surgery but opened after the patients were transferred out of the operating room. Of the nine gastric vessels identified five definitively identified as short gastric arteries. One was identified as the gastric duodenal artery and three were identified as unspecified gastric vessels. The narrative for the single MDR reported as death for the product called LBK narrative indicated that the device was not in contact with the patient and that the death was not device related."

Dr. Harris: Very helpful, thank you. And can you elaborate on this information?

Dr. Chen: Thank you for that summary and I also want someone from our team to chime in on this. Cal, can you elaborate on this information?

Dr. Rabang: Cal Rabang, FDA Division of General Surgical Devices. Dr. Galandiuk, thank you for the that information, that pretty much sums up the narrative that we wanted to share. Yes, the 13 were device-related used for the sealing of vessels of which the 12 you mentioned had vessels that appeared to have opened following the surgical procedure.

Dr. Harris: For those of you who may not be familiar with the ultrasonic scalpels, which are frequently used for dividing these vessels, manufacturers do at times give guidance around what size vessels should be sealed with these devices and secondly, there's potentially concern that the seal is obviously not adequate and doesn't hold over time. These are slightly different performance-related questions than what I think we've been talking about. Not about device fracturing, per se, but may be to insufficient inadequate energy delivery or device having a broader tolerance in terms of its performance and the way it is impacting the tissue than predicted.

I don't know whether that's captured by any of these special controls or not, but when talking again about the thermal behavior for the performance of the devices, I am assuming that they certainly should be able to give guided data and consistency with which that energy is applied and the around which it will be impacting. Dr. McGrath, you have your hand up literally.

Dr. McGrath: It is interesting that 12 of them were in the abdomen, they weren’t with neurosurgical applications, which takes us back to my comment to what my comment was a long time ago. The list of special requirements, the HC – the detailed summary of procedure-related complications. I do think that piece about the use of the abdomen needs to be laid out more clearly. You just commented, Dr. Harris, that there is some specificity about how large a vessel, but again, I don't know if it's a challenge to the device or a challenge to the user to understand the

limitations of what they are using, and so I think that little piece needs to possibly be more robustly drawn out since this is a very focused thing on the abdomen. Thank you.

Dr. Chen: This is Long Chen. Can I elaborate on that? Thank you for the comments. This is talking about one type of performance testing data that we are looking into, called the vessel sealing. And yes, you are absolutely right. For the Agency, when we go through the review process, we do have a limitation on a so called – based on the performance test data they provided. To the degree of size of the vessel, the device can be useful. For example, up to 3 millimeter or five millimeter or up to seven millimeter of vessel sealing. And it is evaluated through the performance testing data, and it is also required to be incorporated in the labeling for the device.

Dr. Harris: Thank you. Dr. Galandiuk.

Dr. Galandiuk: It's also I think odd that these patients should have – I mean, after any kind of surgery, there's bleeding and patients can be taken back to the operating room for bleeding. I find it is hard without any other circumstances listed is knowing why these patients died of postoperative bleeding. Frequently in recovery room, patients' blood pressures may be higher, and hypertension can cause re-bleeding. You could have problems with coagulopathy causing, you know, re-bleeding.

And patients can be unobserved and bleed a lot and causing more problems with coagulopathy it's kind of unclear. Sometimes people will appropriately use the harmonic scalpel or other energy sealing devices, pulling tissues very taught and they don't work as well. So, a lot of factors and improper use doesn't necessarily mean the device is failed or you have a larger

vessel and might seal it twice before cutting through, and you can't necessarily say because it is bleeding, it's a device failure.

Dr. Harris: I agree. I think that we have all seen staplers fail and usually it is much more obvious, because the staples didn't fold or bend. But here I agree, it'd be very hard to tease apart how much was operator dependent, disease dependent and or device dependent. And I think Dr. Bryant's comment, as I recall talking hundreds of thousands if not in the millions of applications, the denominator would be quite large here. Dr. Bryant, does that satisfy your request for more information in that regard?

Dr. Bryant. It does. Thank you, Dr. Harris.

Dr. Harris: Any other questions from the panel? We're discussing whether we support the proposal from the FDA to regulate this class of devices as Class II with this special control and specifically the opportunity to address the rigor and granularity of those controls where we have particular concerns.

So to summarize for Dr. Krause, I think the committee does support the classification of these devices for their regulation as Class II, and you have heard robust discussion regarding concerns around use-life, making sure the animal models, for which these are tested are appropriate and that the labeling for various procedures be sufficiently specific, and other – it seems as though there are some concerns voiced about making sure the performance testing perhaps even be at the level of each individual device prior to its sale, and that the performance testing be sufficiently rigorous and we won't find these instruments being sold at Walmart. Any other questions from the panel? Is that sufficient for you Dr. Krause?

Dr. Krause: Thank you. I appreciate all of the discussion, which I think is extremely valuable for FDA. I am representing one of our offices, and I think for our purposes, that it was all sufficient, but I want to make sure the neuro group is also satisfied, so Sergio, can you please weigh in as to whether you believe the discussion was adequate for your group as well?

Mr. Castillo: Certainly, I am Sergio de del Castillo. I am the Associate Director for Policy in the Office of Neurosurgical and Physical Medicine Devices. Yes, we are satisfied with the information we received from the panel. Thank you.

Dr. Harris: Thank you. So, at that time, I would like to ask our representatives, Ms. Rachel Brummert, our consumer representative Dr. P. Lamont Bryant, and our industry representative, and Ms. Sonia Morris, our patient representative if they have additional comments. Ms. Brummert.

Ms. Brummert: I don't have any additional comments.

Dr. Harris: Thank you, Dr. Bryant.

Dr. Bryant. As always, I sit on these panels, and patients are always at the center and I think they're well represented by both the officers of FDA through their presentations, the preparation for these presentations, the depth, and the, I guess the passion of the conversation that we had specifically with the panel. I would just like to say I'm really humbled to be a part of this process, and thank you for all your work and, your leadership.

Dr. Harris: Thank you Dr. Bryant. Ms. Morris.

Ms. Morris: My reception is really bad. I enjoyed it. It was my first panel and didn't really know what to expect. It is kind of overloading, but it is a good experience and I enjoyed it.

Dr. Harris: Thank you for your participation. At this time the panel will hear summations, comments, and clarifications from FDA. Dr. Krause.

Dr. Krause: Well, I would like it to say that the FDA appreciates all the input from all of the panel members. I think everything was definitely important information, and we will take it to heart, and we will use it to further instruct our, you know, device special controls that we will develop. I would like to thank you, Dr. Harris, for your excellent leadership of this panel. I would like to thank our patient industry and consumer representatives for their reps for their work. I'd like to thank all of the expert panel members who providing us with their recommendations and thoughts for the last couple of days. I would like to thank the individuals who spoke on the open public hearings on day one.

And also thank all of our FDA staff who did such an excellent job preparing for this meeting. So, thank you all and it is been a pleasure.

Dr. Harris: At this time, are there any final comments from the panel members? If not, I would like to add my thanks to those of Dr. Krause, to the members of the panel, to the FDA, to the participates in the open public hearing for their contributions and consequently, this meeting of the Medical Devices Panel is now adjourned.