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DEPARTMENT OF HEALTH AND HUMAN SERVICES

FOOD AND DRUG ADMINISTRATION

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CENTER FOR DEVICES AND RADIOLOGICAL HEALTH

MEDICAL DEVICES ADVISORY COMMITTEE

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NEUROLOGICAL DEVICES PANEL

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June 4, 2021
9:00 a.m.

Via ZOOM Videoconference

PANEL MEMBERS:

MARY JENSEN, M.D.	Temporary Panel Chair
EARL RAY DORSEY, M.D., M.B.A.	Voting Member
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STEPHEN McDAVITT, PT, DPT, M.S., FAAOMPT, FAPTA	Temporary Voting Member
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DAVID J. KENNEDY, M.D.	Temporary Voting Member
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WAYNE GOODMAN, M.D.	Temporary Non-Voting Member
HEATHER ADAMS, Ph.D.	Temporary Non-Voting Member
ROBERTO ORTIZ-AGUAYO, M.D., M.M.M.	Temporary Non-Voting Member
JAMES JOHN McGOUGH, M.D.	Temporary Non-Voting Member
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M E E T I N G

(9:02 a.m.)

DR. JENSEN: I would like to call to order the FDA's Center for Devices and Radiological Health Neurological Devices Panel of the Medical Devices Advisory Committee on June 4th, 2021. It is now 9:00 a.m.

I'm Dr. Mary Jensen, the Chair of the Panel. I'm an interventional neuroradiologist and a professor at the University of Virginia. My specialty is endovascular treatment of ischemic and hemorrhagic stroke.

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

For today's agenda, during Session I, the Committee will discuss and make recommendations regarding the classification of attention task performance recorders, which are currently unclassified preamendment devices, to Class II (general and special controls).

During Session II, the Committee will discuss and make recommendations regarding the classification of optical contour sensing devices, which are currently unclassified preamendment devices, to Class I (general controls).

During Session III, the Committee will discuss and make recommendations regarding the classification of plunger-like joint manipulators, which are currently unclassified preamendment devices, to Class II (general and special controls).

FDA is convening this meeting to seek expert opinion on the classification of these devices.

I want to lay down a few ground rules in this virtual environment. If a panelist wants to ask a question, please use the hand-raising function on your Zoom platform and I will get

to your questions as we proceed through the day. Alternatively, you can raise your hand, too, and I will see you on the screen and recognize you. We want to prevent multiple persons from speaking over each other as we proceed, as this entire meeting is being transcribed for the official record.

Before we begin, I would like to ask our distinguished Panel members and FDA staff attending virtually to introduce themselves. When I call your name, please state your area of expertise, your position and affiliation.

Dr. Patrick Lyden.

DR. LYDEN: Good morning, I'm Pat Lyden. I'm a neurologist at USC in Los Angles, and my area of specialization is stroke research.

DR. JENSEN: Thank you.

Dr. Julie Pilitsis.

DR. PILITSIS: Hi, my name is Julie Pilitsis. I'm a neurosurgeon in Albany, New York, and my area of expertise is chronic pain and neuromodulation.

DR. JENSEN: Thank you.

Dr. Karen Johnston.

DR. JOHNSTON: Hi, good morning. My name is Karen Johnston, I'm a vascular neurologist at the University of Virginia.

DR. JENSEN: Thank you.

Dr. Earl Ray Dorsey.

DR. DORSEY: Good morning, Dr. Jensen. My name is Ray Dorsey, I'm a neurologist at the University of Rochester where I direct the Center for Health and Technology.

DR. JENSEN: Thank you.

Mr. Elijah Wreh.

MR. WREH: Hi, everyone. My name is Elijah Wreh and I'm the representative from

industry and I work for Zimmer Biomet. My area is regulatory affairs.

DR. JENSEN: Thank you.

Ms. Veverly Edwards.

MS. EDWARDS: Hi, my name is Veverly Edwards. I'm a Consumer Rep for FDA and a patient safety advocate.

DR. JENSEN: Thank you.

Dr. Sujay Galen.

DR. GALEN: Good morning, Dr. Jensen and fellow panelists. I am a chair of the department of physical therapy at Georgia State University, Atlanta, Georgia, and my area of expertise is in wearable technology and also in any physical therapy intervention and outcome measures. Thank you.

DR. JENSEN: Thank you.

Dr. Stephen McDavitt.

DR. McDAVITT: Good morning, I'm Steve McDavitt. I'm a physical therapist, a full-time practicing PT. I also work at South College in Knoxville, Tennessee, as assistant professor. Thank you.

DR. JENSEN: Thank you.

Dr. Rory Cooper.

DR. COOPER: Hello, I'm Dr. Rory Cooper and I'm the FISA and Paralyzed Veterans of America Distinguished Professor at the University of Pittsburgh and a senior research career scientist in the U.S. Department of Veterans Affairs, and I am a bioengineer specializing in medical devices.

DR. JENSEN: Thank you.

Dr. David Kennedy.

DR. KENNEDY: Good morning, everyone. My name is D.J. Kennedy, I'm Professor

and Chair of Physical Medicine and Rehabilitation at Vanderbilt University Medical Center. My area of expertise is spine, interventional spine and physical medicine and rehabilitation.

DR. JENSEN: Thank you.

Dr. Karen Anderson.

DR. ANDERSON: Hi, I'm Karen Anderson. I'm a Professor of Psychiatry and Neurology at Georgetown University, and my area of expertise is clinical trials and neurodegenerative disease.

DR. JENSEN: Dr. Wayne Goodman.

DR. GOODMAN: Hi, I'm Wayne Goodman. I'm a psychiatrist with an undergraduate degree in electrical engineering. I'm currently professor and chair of the Department of Psychiatry at Baylor College of Medicine, and my expertise is in both the psychopharmacology and neuromodulation of neuropsychiatric disorders.

DR. JENSEN: Thank you.

Dr. Heather Adams.

DR. ADAMS: Good morning, everyone. I'm Heather Adams, I'm a pediatric neuropsychologist at the University of Rochester Medical Center in Rochester, New York. My area of expertise is pediatric neurodevelopmental and neurodegenerative disorders.

DR. JENSEN: Thank you.

Dr. Roberto Ortiz-Aguayo.

DR. ORTIZ-AGUAYO: Hi, good morning. I'm Roberto Ortiz, I am associate chair of the department of psychiatry at Children's Hospital, Philadelphia, where I'm a pediatrician and child psychiatrist and my area of expertise is psychosomatic medicine.

DR. JENSEN: Thank you.

Dr. James McGough.

DR. McGOUGH: Good morning. It's Jim McGuff (ph.). I'm a child psychiatrist and

professor at UCLA, and one of my main areas is with genetics and intervention trials for ADHD.

DR. JENSEN: Thank you.

Dr. Randy Trumbower.

DR. TRUMBOWER: Good morning, my name is Randy Trumbower. I'm an assistant professor at Harvard Medical School and I'm also the director of the spinal cord injury division at the Spaulding Rehab Hospital in Boston, Massachusetts. Much of what I do is study the way humans move and how spinal injury affects or causes corruption of these movements.

DR. JENSEN: Thank you.

Dr. Vivek Pinto.

DR. PINTO: Vivek Pinto, I'm the director for Division 5 B in the Office of Neurological and Physical Medicine Devices. My division is the division for neuromodulation and physical medicine devices.

DR. JENSEN: Thank you.

Dr. Lin Zheng.

DR. ZHENG: Hi, I'm Lin. Can you hear me?

DR. JENSEN: Yes.

DR. ZHENG: Just testing. Good. I'm Lin Zheng, I'm the division director for Division 5 A, that includes neurosurgical, neurointerventional, and neurodiagnostic devices, in the Office of Neuro and Physical Medicine.

DR. JENSEN: Thank you.

Dr. Christopher Loftus.

DR. LOFTUS: Yeah, good morning and thank you. My name is Christopher Loftus, I'm a Professor of Neurosurgery at Temple Medical School in Philadelphia and I am the acting

director of the FDA's OHT 5.

DR. JENSEN: Thank you.

Dr. Jane Peng.

DR. PENG: Good morning, everyone. So I'm a medical officer in FDA, a neurologist, subspecialty as epileptologist, so I have a Ph.D. in neuroscience by training. Thank you.

DR. JENSEN: Thank you.

And Commander Patricio Garcia.

CDR GARCIA: Good morning, everyone. My name is Patricio Garcia and I'm the Designated Federal Officer for this meeting. Thank you.

DR. JENSEN: Thank you.

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

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

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

FDA has determined that members and consultants of this Panel are in compliance with Federal ethics and conflict of interest laws. Under 18 U.S.C. Section 208, Congress has authorized FDA to grant waivers to special Government employees and regular Federal employees who have financial conflicts when it is determined that the Agency's need for a

particular individual's services outweighs his or her potential financial conflict of interest.

Related to the discussion of today's meeting, members and consultants of this Panel who are special Government employees or regular Federal employees have been screened for potential financial conflicts of interest of their own as well as those imputed to them, including those of their spouses or minor children and, for the purpose of 18 U.S.C. Section 208, their employers. These interests may include investments; consulting; expert witness testimony; contracts/grants/CRADAs; teaching/speaking/writing; patents and royalties; and primary employment.

For today's agenda, during Session I, the Committee will discuss and make recommendations regarding the classification of attention task performance recorders, which are currently unclassified preamendment devices, to Class II (general and special controls).

During Session II, the Committee will discuss and make recommendations regarding the classification of optical contour sensing devices, which are currently unclassified preamendment devices, to Class I (general controls).

During Session III, the Committee will discuss and make recommendations regarding the classification of plunger-like joint manipulators, which are currently unclassified preamendment devices, to Class II (general and special controls).

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. Section 208.

Elijah Wreh is serving as the Industry Representative, acting on behalf of all related industry. He is employed by Zimmer Biomet.

We would like to remind members and consultants that if a discussion involves 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 that they may have with any firms at issue.

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

For the duration of the Neurological Devices Panel Meeting on June 4, 2021, Drs. Heather Adams, James McGough, and Roberto Ortiz-Aguayo have been appointed to serve as Temporary Non-Voting Members.

For the record, the following individuals serve as consultants to advisory committees in the Center for Drug Evaluation and Research: Dr. Adams is a consultant to the Gastrointestinal Drugs Advisory Committee, Dr. McGough is a consultant to the Psychopharmacologic Drugs Advisory Committee, Dr. Ortiz-Aguayo is a member of the Pediatric Advisory Committee in the Office of the Commissioner.

These individuals are special Government employees who have undergone the customary conflict of interest review and have reviewed the material to be considered at this meeting.

The appointments were authorized by Russell Fortney, Director, Advisory Committee Oversight and Management Staff, on May 26th, 2021.

DR. JENSEN: Thank you, Commander Garcia.

We're now going to begin the meeting with this Open Public Hearing portion of the meeting. Public attendees are given an opportunity to address the Panel, to present data, information, or views relevant to the meeting agenda. We have no Open Public Hearing speakers today, so we're going to move on to the first presentation.

Ms. Megha Reddy will present on the FDA classification and reclassification overview.

Ms. Reddy, please proceed.

MS. REDDY: Hello, my name is Megha Reddy 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 and reclassification processes which form the basis for the discussions over the next day.

The purpose of this Panel will be regarding the classification of devices that are currently unclassified. Specifically, for six preamendment devices, unclassified device types, the Panel will be asked to provide input to the FDA on the appropriate classification (Class III, Class II, or Class I) for each device type.

Let's start by explaining the different classes of medical devices. Devices are classified based on the controls necessary to mitigate the risks associated with the device type. Class I devices are only subject to general controls. Class II devices are subjected to both general and special controls. And Class III devices are subjected to general controls and premarket approval. These regulatory controls will be discussed in greater detail in the following slides. Importantly, 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 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 include meeting established registration and device listing requirements, following good manufacturing practices, adhering to recordkeeping 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 this slide you can see a few examples of Class I devices.

These include hospital beds, ventricular needles and anvils used to form skull plates, and certain manual surgical instruments.

There is also an alternate 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 cannot -- 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 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 neurostimulators, aneurysm clips, and blood clot retrievers.

Typically, Class II devices require a premarket notification, generally 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 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 the general and special controls are sufficient to provide reasonable assurance of 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 application, or a PMA, prior to being marketed. Examples of Class III devices include pacemakers, implanted neurostimulators, and deep brain stimulators.

Here you can see a flowchart which walks through the general decision-making process for each of the classes that was just discussed. We start with determining whether general controls are sufficient. If so, the device could be appropriately regulated in Class I. If not, we ask whether there is sufficient information that allows us to be able to develop special controls. If so, the device can be appropriately regulated in Class II. If not, then it will 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 for unreasonable risk of illness or injury. If the device is not life-supporting or life-sustaining, or if it is of substantial importance in preventing impairment of human health and does not present a potential unreasonable risk of illness of injury, then we end up back at the Class I designation.

Now we will shift our focus to the classification process for the preamendments unclassified device types which will be discussed today and tomorrow. Before we walk through the process, here are a few quick definitions.

First, what is a preamendments device? A preamendments device is a device which was introduced into interstate commerce prior to May 28th, 1976 or the date of the enactment of the Medical Device Amendments to the 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 second purpose of this Panel meeting, to formally classify these unclassified devices. Please note that while these devices are not classified, they are currently brought to market through the 510(k) process.

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.

Second, 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, FDA will publish a final rule classifying the device.

What we ask from the Panel today is to provide input on the classification of these unclassified device types and whether they should be classified into Class III, Class II, or Class I. The input should include an identification of the risks to health presented by the device; a discussion of whether the device is life-supporting, life-sustaining, of substantial importance in preventing impairment of human health or if it presents a potential unreasonable risk of illness or injury; a discussion of whether sufficient information exists to develop special controls, an identification of those special controls, and a discussion of whether general controls are sufficient by themselves.

Following this Panel meeting, 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 Register* 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 devices can be appropriately regulated as Class I or Class

II devices, the devices may continue to be marketed. However, if 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. If this PMA is not approved, the devices will be considered misbranded and must be removed from distribution.

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

DR. JENSEN: Thank you very much. I'd like to thank Ms. Reddy for her presentation.

Does anyone on the Panel have any questions for Ms. Reddy?

(No response.)

DR. JENSEN: All right, I don't see anybody raising their hand, so we're going to move on and start with the presentation on attention task performance recorder. Dr. Mohua Choudhury will present on this device, these devices.

Ms. Choudhury, would you please proceed?

DR. CHOUDHURY: Good morning, my name is Mohua Choudhury 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 the effort to classify attention task performance recorders under product code LQD. These devices are currently unclassified and we are soliciting your feedback on the appropriate regulatory classification for these devices.

Here is the outline for today's presentation. These are the items that we will be discussing.

Attention task performance recorders are used to measure reaction time in response

to attention tasks. They may or may not be used to aid in the assessment or diagnosis of specific clinical conditions, most specifically attention deficit hyperactivity disorder or ADHD.

For general assessment of reaction time, the device may provide measures of both the speed of responding to stimuli and how accurately patients respond to stimuli without specific use and without providing clinical context regarding a specific disease or condition.

For the assessment of specific clinical conditions such as ADHD, the device may additionally provide information regarding correlation with known neuropsychometric tests or aspects of cognition related to the condition of interest.

Attention task performance recorders are typically software based, with a test or evaluation being manually administered by a clinical end user for assessment of the symptoms of interest.

Examples of indications for use statements for cleared attention task performance recorders are provided here. Types of uses that have received clearance to date typically involve providing objective measures of reaction time, or objective measures of symptoms associated with ADHD, such as hyperactivity, impulsivity, and inattention.

The attention task performance recorder is a preamendments, unclassified device type. This means that this device type was marketed prior to the Medical Device Amendments 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 LQD product code. Hence, the purpose of today's Panel meeting is to create a classification for this product code.

To date, there have been 11 attention task performance recorders cleared through

the 510(k) pathway under the LQD product code, the first clearance occurring in 1986 and the last in 2018. All devices are indicated for prescription use. Please refer to Section 2 of the Executive Summary for a list of cleared devices under product code LQD.

The vast majority of cleared attention task performance recorders are intended to aid in the assessment of ADHD. ADHD is a neurodevelopmental disorder characterized by the following core symptom domains: inattention, hyperactivity, and impulsivity.

ADHD primarily affects children and adolescents ages 2 to 17 years of age. Clinical presentation of symptoms changes with patient age, with the types of ADHD differing as dependent on the predominant symptoms per subject.

ADHD is considered to be symptom complex, as causes can be due to a variety of influences and result in a range of presenting behaviors or symptoms.

Given the variation in causes and behavioral consequences of ADHD, there is no single test used to diagnose the disorder. Clinician judgment is currently the most widely accepted method of assessment. This typically involves gathering observational information and using tests of behavior and neuropsychological functioning.

However, there is limited clinical guidance regarding the combination of measures that should be used in the diagnostic assessment of ADHD. Use of this approach is further limited given reliance on subjective measures such as interviews, leading to discrepancies in diagnosis.

Objective measures of associated symptoms, as incorporated in some of the devices cleared using the LQD product code, have a potential to augment and streamline current practice.

We conducted a literature review to identify any published information between January 1st, 2010 and December 31st, 2020 regarding the safety and effectiveness of attention task performance recorders. Searches were limited to publications in English and

excluded conference proceedings and abstracts. A total of 42 articles covering 41 studies were selected for review based on their relevance to the reported safety and/or effectiveness of these devices. I'll briefly summarize some of the main take-home points from each of the review articles.

With respect to safety, the search did not identify literature reported on adverse events related with the use of attention task performance recorders.

With respect to effectiveness, the studies primarily evaluated different uses of the product for evaluation of reaction time or aiding in the clinical assessment of ADHD or in the evaluation of treatment interventions in patients with ADHD.

With respect to assessing reaction time, 8 of 13 studies identified evaluated use of the DANA product and the remaining five evaluated use of the Dynavision product. The studies summarized that the effectiveness of the DANA product in measuring reaction time reliably is supported. However, there's greater uncertainty associated with use of the Dynavision product.

With respect to cognitive assessment, two studies identified evaluated use of the Fagan test. Both studies presented conflicting results in terms of the effectiveness of the Fagan test in differentiating normal and abnormal cognitive skill levels.

With respect to aiding in clinical assessment of ADHD, one systematic literature review, one meta-analysis, and 12 studies identified evaluated use of the Gordon Diagnostic System or GDS, the QbTest, the OPTAx System, and the T.O.V.A. product, with the majority of findings involving use of the GDS or QbTest. Findings supported that both the GDS and QbTest products demonstrated greater accuracy when used in combination with other rating scales. Additionally, the QbTest product demonstrated good convergent and discriminant validity when comparing to rating scales used in diagnostic assessment of ADHD.

With respect to aiding in the evaluation of treatment interventions to ADHD, one systematic literature review and 17 publications which reported on 15 studies total were identified. Of the reported studies, 5 of 15 evaluated use of the tests of variables of attention, or T.O.V.A., and 10 of 15 evaluated use of the QbTest. While the effectiveness of the QbTest in capturing statistically significant improvement in core ADHD symptoms is supported, the T.O.V.A. product demonstrated limited sensitivity to medication effects and group-specific differences in objective measures of reaction time post-intervention.

In summation, the search did not identify literature reporting on adverse events related to the use of attention task performance recorders.

Given the heterogeneity of the use of the type of product, it is challenging to draw conclusions regarding effectiveness.

Other limitations that limit the ability to draw conclusions regarding the effectiveness of these products are the sample size of the studies identified, conduct of studies outside the U.S., and limitations associated with both use and interpretation of rating scales and adult self-report, such as variation in parent or caregiver and teacher interpretation and recall of patient behavior and cultural interpretation of rating scales. All of these factors can affect the generalizability and validity of the assessment results.

The Medical Device Reporting or MDR system provides FDA with information on medical device performance from patients, healthcare professionals, consumers, and mandatory reporters including manufacturers, importers, and device user facilities.

The FDA receives MDRs of suspected device-associated deaths, serious injuries, and certain malfunctions. The FDA uses MDRs to monitor device performance, detect potential device-related safety issues, and contribute to benefit-risk assessments of these products.

MDRs can be used effectively to establish a qualitative snapshot of the adverse events for a specific device or device type, and detect actual or potential device problems

used in a real-world setting or environment.

Although MDRs are a valuable source of information, this passive surveillance system has limitations including the submission of incomplete, inaccurate, untimely, unverified, duplicated or biased data. In addition, the instance or prevalence of an event cannot be determined from this reporting system alone due to potential underreporting of events and lack of information about the frequency of device use. Finally, the existence of an adverse event report does not definitively establish a causal link between the device and the reported event. Because of these limitations, MDRs comprise only one of the FDA's tools for assessing device performance. As such, MDR numbers and data should be taken in the context of the other available scientific information.

To further contribute to the benefit-risk assessment of attention task performance recorders, the Manufacturer and User Facility Device Experience, or MAUDE, was reviewed for MDRs for the attention task performance recorders cleared under product code LQD without time constraints. No MDRs were reported.

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 recall classification may occur after the firm recalling the medical device product conducts and communicates with its customers about the recall. Therefore, the recall information posting date identified on the database indicates the date FDA classified the recall. It may not reflect the date when the recall was first initiated by the firm.

Recalls were reviewed using the medical recall database without time constraints. No recalls were reported for attention task performance recorders.

To determine the appropriate classification for attention task performance

recorders, we have identified risks associated with these devices and possible mitigations for these risks. We will be asking the Panel for input on the lists of risks and mitigations.

Since the MAUDE database did not contain any relevant MDRs, we relied on information available to FDA regarding cleared devices and the articles from the previously discussed literature review to identify risks associated with these devices. The identified risks we've identified for attention task performance recorders differ across the uses of the device, which are split into two separate categories.

For attention task performance recorders intended to measure reaction time and associated patient performance in response to attention tasks only, without aiding in assessment or diagnosis, the two risks are: patient discomfort, which can result from visual or mental fatigue due to confusion of tasks performed during assessment; incorrect or inaccurate measurement of reaction time or other attention tasks, which can result from use-based errors related to data collection and use, and interpretation of the results obtained.

For the second intended use category, attention task performance recorders intended to aid in the assessment or diagnosis of specific diseases or conditions, the two risks are: patient discomfort, which can result from visual or mental fatigue due to confusion of tasks performed during assessment; incorrect or inaccurate results, both of which could result in inappropriate therapy or delay in treatment which can result from use-based errors related to data collection and use, and interpretation of the results obtained.

For both uses of this device, we propose that these risks will not be sufficiently addressed by general controls and therefore require special controls as per the device regulation process.

Here is our proposed classification regulation for attention task performance

recorders, which is split based on the intended uses of the device. We will be asking the Panel for input regarding the proposed classification and special controls required to mitigate the identified risks to health.

Part (a) of the regulation identifies and defines an attention task performance recorder as a device intended to measure reaction time and associated patient performance in response to attention tasks. The device may or may not be used to aid in the assessment of specific clinical conditions.

Part (b) of the regulation defines the classification and states the special controls for both intended uses of the product. In Part (b)(1), for use to measure reaction time and associated patient performance in response to attention tasks only without aiding in assessment or diagnosis, we are proposing classification as Class II devices with special controls specific to the device hardware, software, nonclinical performance evaluation, and labeling.

In Part (b)(2), for use to aid in the assessment or diagnosis of specific diseases or conditions, we are also proposing classification as Class II devices with special controls. In addition to meeting the controls specific to the device hardware, software, and nonclinical performance evaluation that was identified in the previous slide for the first intended use category, as denoted by the red text on this slide, we are also proposing additional controls specific to clinical performance evaluation for devices falling under this intended use.

In addition to the previously linked controls identified for the first intended use category, as denoted by the red text on this slide, we are also proposing inclusion of information regarding clinical performance evaluation in the labeling and other labeling controls for the purpose of additional risk mitigation.

This concludes our presentation. Thank you so much for your time and attention and your thoughtful feedback on the following Panel questions.

DR. JENSEN: Thank you very much for that excellent presentation.

I want to open the floor to the experts around the table to begin deliberating on attention task performance recorders, considering your expertise, everything you have read in your panel packs, and heard in today's Open Public Hearing and from the presentations. Who would like to start? How about our experts who actually treat these patients and have experience with these devices?

Dr. McGough.

DR. McGOUGH: Right. So this is sort of my thing, so let me just weigh in. I've never been on a panel like this, it's an amazingly diverse group, so I appreciate -- and what a bunch of experts, so I appreciate being part of this today.

As with mostly everything, as with everything in psychiatry, ADHD is a behavioral syndrome of heterogeneous brain etiology. We do not yet completely understand, you know, at all what's going on in the brain.

The sensitivity and specificity of these tests are not high, and our work -- and we're one of the leading centers looking at these executive functioning deficits in people diagnosed with ADHD. Only about half of the people actually score in a disabled range, so even at the get-go you're only going to catch about half of the people. I think the FDA's comments were right on target. I mean, maybe there's some discomfort, there's certainly no great medical risk to the procedure. The problem is that the sensitivity and specificity are just not good. So, as they suggest, you can miss cases. You can also misdiagnose cases.

I think their language really suggesting that this is not a standalone measure is absolutely appropriate. I think their general recommendation is pretty much on target. I don't actually see much added value to the test, myself, they've never been predictive of treatment outcome. As I said, they really are not particularly predictive of diagnosis, as well. Of course, psychiatrists are always trying to be like other medical physicians and they

love the idea of objective lab tests. This is another one that is not one of those, but it is certainly sometimes perceived as such. That's the main risk. But beyond some misclassification, I think the FDA is -- actually, I think they're absolutely correct in what the risk of the device is.

DR. JENSEN: So do any of the other panelists see any other risks that Dr. McGough didn't outline with the device?

Dr. Adams.

DR. ADAMS: Yeah. Hi, this is Heather Adams. Dr. McGough, it's great to hear from you and I'm just so excited to be in a room with you, even virtually.

So I completely agree. I'm a pediatric nurse psychologist, also a clinical child psychologist, I see a lot of children who have ADHD. I have never used these devices clinically, for exactly the reasons Dr. McGough outlined.

You know, one of the key components of the diagnosis is that children have to demonstrate in pyramids in at least a couple of settings, you know, everyday settings, and one of the problems of these devices is it assesses children completely that are removed from how they feel and function in their everyday settings. So that's a big challenge.

I think there was one other risk that I had wondered about with these devices, which has to do with the potential loss of confidentiality or privacy. When these software programs are used, it's often necessary to enter a child's date of birth and date of evaluation so that some values can be generated in comparison to age-based norms and more and more of these -- you know, the devices and the companies that administer them are moving to cloud-based systems and so that information is kind of getting out there and has to be maintained in a secure way. Again, I don't think there is a medical harm to a child for completing one of these tasks, but it's just one of those maybe additional risks that I might think about if somebody's information is being collected.

You know, another risk, I think, which is not directly device related, has to do with just the financial burden or financial cost. I would be concerned that these could be added as part of a diagnostic workup when it has been clearly expressed by Dr. McGough, they're not really needed if you do a good diagnostic evaluation of a child following the evidence-based guidelines that have been outlined. And so I just would be concerned about these being added to assessments and workups and adding unnecessary cost to families.

DR. JENSEN: Thank you, Dr. Adams.

Dr. Lyden.

DR. LYDEN: Yeah, I have a question for Dr. McGough and Adams and the others that actually treat these patients. A two-part question. The first part is yesterday we heard about completely different types of devices for which the evidence was one-millionth of the evidence that we have on these devices today and where there was evidence, it was very clear the devices didn't function at all. I'm hearing you say these devices are so-so but really don't complement or replace a good examination by an expert practitioner. Here in Los Angles, our problem is access. We have far more children that need to be evaluated, and young adults, than there are clinicians willing to see them.

Are these devices good enough that in the hands of a general practitioner they could at least give some indication towards a diagnosis that would at least be an interim solution until my patient can get in to see one of you?

DR. McGOUGH: I think the problem, again, is that the sensitivity and specificity is like 50%. We also have to recognize we live in a world where kids spend two-plus hours a day on Nintendo, so they've gotten really good at these games and again, the devices just don't pick up the problem. A better method would be to simply implement a use of behavioral rating scales and screens, that's more of the standard. Those are very well normed and can certainly show you if a person is outside. It's cheap, it takes 5 minutes for

a parent to fill out in your waiting room, and it takes 15 seconds for you to look at it and say yeah, I need to ask a few more questions here and I can probably start treatment. So there's not a lot of added value. It's a bit pseudoscience relying on these things. I always kind of laugh when I see people coming in with these results. It's not really harmful, but it's expensive, and I think it gives people some false sense of security.

DR. ADAMS: Yeah, I agree. There was a paper published a few years ago in the *American Academy of Child and Adolescent Psychiatry*, I think Jarrett (2018), Ollendick was the senior author, that looked at the incremental validity of a different task like this, the Conners' Continuous Performance Test, which is very similar in how it's utilized in relation to things like rating scales such as the Vanderbilt or Conners' Parent Rating and Teacher Rating Scales, and really didn't find much incremental validity.

And so I think, again, it just underscores the fact that there's not a lot of added value to using these. Again, sensitivity and specificity are not great. And the American Academy of Pediatrics has also already published really good practice parameters for general practitioners that they can follow to make the diagnosis in the general setting. You know, for garden variety ADHDs specialty care probably isn't needed to do the assessment and diagnosis.

DR. JENSEN: Dr. Ortiz, did you have a question?

DR. ORTIZ-AGUAYO: No, actually Dr. Adams addressed what I was going to say in terms of the public health aspect of this and the reality that the majority of ADHDs are diagnosed and managed at the level of general pediatrics and, as she mentioned, the American Academy of Pediatrics has very robust tools for the clinicians to do this and it's actually core requirements for training.

One thing that I did have a question about -- well, two. One is procedural to what we're doing today, which is we are -- we're not talking about removing these devices from

the market, we are talking about they exist, they're already out there, they're properly classified, right? But our, you know --

DR. JENSEN: Our job is to help the FDA determine what classification the device belongs in and we're focusing on safety and efficacy, and I think so far what I'm hearing from the panelists is that the device is essentially safe, the patients aren't getting shocked by it or anything like that.

DR. ORTIZ-AGUAYO: Um-hum.

DR. JENSEN: The question is how does the efficacy fall into it, right?

DR. ORTIZ-AGUAYO: As Dr. Lyden mentioned, yesterday -- it's better numbers than we saw yesterday but there's no added value and to me, the primary risk, as Dr. McGough mentioned, is delaying treatment along with any potential undue distress on the families or financial distress.

There was something in the Executive Summary that I did want to ask the reviewers about, which was the use of some of these devices in concussion and in potential detection of subclinical concussion, because that brought my eye a little bit more than the utility for ADHD.

DR. JENSEN: Can I have our reviewer discuss that portion of the evaluation?

DR. ZHENG: Dr. Jensen, this is Lin. I'm going to turn to -- if I can invite Mr. Jay Gupta to sit in for that question. Jay is the assistant director for the neurodiagnostic devices team.

DR. JENSEN: Thank you. Dr. Gupta.

MR. GUPTA: Yeah. Hi, folks. Can you hear me okay?

DR. JENSEN: Yes.

MR. GUPTA: Yeah, so these products are not specifically cleared or intended to be used to aid in the assessment of concussion or any aspects of concussion. We do have other neurocognitive task batteries that are computerized that are intended for that

purpose, but those are regulated separately. These specific products are intended only for the assessment of attention and specifically, the only diseases or conditions that are specified for use with these is ADHD.

DR. JENSEN: So if someone were to use this device in a post-concussion syndrome, that would be off-label use of the device.

MR. GUPTA: That is correct. Some of these products are -- you know, as we mentioned, they are broadly indicated just for assessing attention or inhibitory control or whatever. And so if a clinician determines that they need to assess that in whatever patient they have before them, that would potentially still be on label but it wouldn't provide specific information related to symptoms of concussion and it wouldn't provide the comparison to a reference database of potentially concussed patients or perform --

(Cross-talk.)

DR. McGOUGH: In the statement, no.

MR. GUPTA: -- in concussed patients.

DR. JENSEN: Thank you.

Dr. Trumbower, do you want to ask your question? You're muted. Yes, I think we can -- you're unmuted now.

DR. TRUMBOWER: I am unmuted?

DR. JENSEN: No, you're good.

DR. TRUMBOWER: Oh, okay. Very good. I just had a question about individuals with a history of epilepsy or anything along those lines, especially if they're doing computer-type evaluations that may involve patterns of visual stimuli that could trigger seizure.

DR. JENSEN: Dr. Gupta, do you have information on that?

MR. GUPTA: We don't have specific information on any risks associated with the visual stimuli as they relate to inducing seizures. That's typically not the type of visual

stimuli that would be associated with these products, but yeah, that is not something we have data on.

DR. JENSEN: Thank you. I have a --

DR. GOODMAN: Can I ask a question?

DR. JENSEN: I'm sorry, Dr. Goodman, is that you?

DR. GOODMAN: Yeah, it's me. There are several of us that have our hands up, so I went first.

(Cross-talk.)

DR. JENSEN: -- participant thing and look at who has their hand up. Okay, good. So Dr. Goodman and then Dr. Anderson and then Dr. Galen.

So Dr. Goodman, why don't you go?

DR. GOODMAN: Yeah. First a disclaimer. I'm not a child psychiatrist and I haven't used these devices but, as an adult psychiatrist, I've often run into patients, adult patients, who may not have had a diagnosis of ADHD as a child but now come and say that they do have ADHD and they would like to be on medications and in some cases I suspect that they're seeking treatment with stimulants, not so much for treatment of a disorder, but for enhancement of performance. So that's one of the concerns we have clinically.

My question, in terms of these devices -- there's several questions. One is are they normed for age or are they just designed for children and adolescents, that's my first question. But I do have a follow-up to that and I wondered, Dr. McGough, if you know the answer or somebody from the FDA knows the answer to that.

DR. JENSEN: So Dr. McGough or Dr. Adams, could you answer Dr. Goodman's first question?

DR. McGOUGH: You know, honestly, I am -- typically, what you get back is an indication that you're in the clinical range and you're not in the clinical range for the test.

That implies it's age normed but honestly, I don't know that. I don't think these have been used broadly in adults with ADHD, but I really don't know. That is a very interesting question. Again, you could -- there's a rating scale called the BRIEF Rating Scale that captures the same thing and it's easily done and that is normed, but I don't know if that would -- I think Dr. Goodman's question would be important to know.

DR. ADAMS: Yeah, so I know that the T.O.V.A. testing only has norms up to about age 17. I'm just looking at the information that the company has on line and it looks like they have a preschool test and a school-age test that -- but oh, no. Actually, they say they have an adult test that goes to age 80-plus. So what the extent of the norms are for that age group or if the norm was as robust as the pediatric groups, I don't know, and we'd have to do a little bit more digging for that. And the BRIEF and the second version, the BRIEF-2, have adult versions as well as child versions that are normed at an age-appropriate cutoff.

DR. JENSEN: Thank you. Dr. Goodman. Did you have --

(Cross-talk.)

DR. GOODMAN: -- answer my question which is related to my initial concern about there might be some patients that illegitimately think they have ADHD and they need medication treatment or some that are seeking a medication treatment. Can one fake results? So in other words, ensure poor performance on reaction time. And is there a way with the test being able to identify those individuals who are not showing effort so that you can identify that these were intentionally bad results? Do we know if there's any way in some of these tests of validating that?

DR. JENSEN: So Dr. Adams or Dr. McGough, do you have any information about that? Dr. Adams.

DR. ADAMS: I could do some digging, but I don't know off hand. A lot of the rating scales actually do have those sort of lie detector questions built in just to look at

consistency of responses or a tendency to amplify responses excessively. I'm not sure if these computerized assessments have those similar checks.

Dr. McGough, do you know?

DR. McGOUGH: I don't think there's -- there's like, not a fake bad scale --

DR. ADAMS: Yeah.

DR. McGOUGH: -- or whatever comes out. I mean, you could go in and just work to blow it, but I don't think this test would be particularly useful. I would not count on this test to give me an indication that this person is malingering. I mean, it's just that there would be other ways to look at that imperfectly, but -- and I think there are much better clinical ways to make a diagnosis in an adult, but -- yeah. No, it would be -- there's nothing in these instruments that's going to give you a signal of that.

DR. ADAMS: Right.

DR. JENSEN: Dr. Goodman. Well, let's let Dr. Goodman make his comment and then Dr. Adams.

DR. GOODMAN: I said that concluded my questions.

DR. JENSEN: Okay. Dr. Adams.

DR. ADAMS: Well, I was just going to add that I work in pediatrics, but my understanding of making the adult diagnoses, it is much more challenging, and part of the challenge is that the symptoms have to have been present during the childhood years and so there's a lot of digging that has to go into gathering that history and trying to connect dots, and so it can't just be based on performance in a moment, there also has to be that arc of development of symptoms having to have been present in childhood.

DR. JENSEN: Thank you.

Dr. Anderson, you have a question?

DR. ANDERSON: Well, actually, I had a comment about the financial burden. To me,

that's one of the main concerns, that parents may pay for these tests and pay a lot of money believing that something technological is somehow much more valuable than the behavioral assessments, which our colleagues tell us they're really the best way to assess these disorders.

Another comment echoing Dr. Goodman's commentary, you know, the diagnosis of ADHD is sometimes sought by parents and students because it gives kids extra time on exams but I'm wondering, is there any worry that these types of assessments would be used to again fake bad or to get the diagnosis of ADHD to have extra time on exams or other accommodations that students and their parents sometimes want?

DR. JENSEN: So I guess one question, is there a risk that this device will be used, or these devices will be used as the only way an individual is diagnosed with ADHD? And therefore there's potential for abuse there as opposed to a complementary device with actual evaluation of patients by a qualified psychiatrist.

DR. McGOUGH: So I think again, let's recognize these have been in the community for decades and some clinicians do do that, they run their T.O.V.A. and then they base it on that. But I think the FDA-proposed labeling is appropriate, it does make it clear. Even the booths at meetings will tell you this isn't the whole thing. So I'm not so worried about that. I mean, people may do it fine but again, no big deal.

I think, in truth, one of my concerns is that the sensitivity is just not great but, based on one who is clinically symptomatic, and I do have test results that show there is delays in response inhibition, for example, that does tend to support my diagnosis. We have other ways of measuring it but if it's there, I would be less concerned about initiating treatment if I was worried about that. The problem is, I think, people could be denied treatment is probably more of the risk. But if they have delays in response inhibition, there is some problem going on. A good clinician would wonder well, is it depression, is it anxiety, there

could also be other explanations, but perhaps there's an incremental bit of support to what you were going to do anyway, but the absence of a finding isn't going to change my thinking.

DR. JENSEN: Okay. Dr. Adams, anything to add with that?

(Off microphone response.)

DR. JENSEN: Dr. Galen, you have a question?

DR. GALEN: Thank you, Dr. Jensen.

And I first of all would say I'm not an expert or I do not treat individuals with ADHD or assess them. My question is more on the technical aspects of the software and hardware of the device, as a biomedical engineer. Given that there's a high rate of errors in reaction time, is there any specified sampling frequency for these devices? Because that's one area where that error could arise. That's number one, so that's a question to the FDA panel.

And I think Dr. Adams mentioned before about confidentiality of how information is stored within these devices, so that's my second concern. And I think both of those risks should be noted by the FDA. Thank you.

DR. JENSEN: Dr. Adams or Dr. McGough or anybody else on the Panel who has --

DR. McGOUGH: So what you get back is errors of omission and errors of commission, so you get people who respond too quickly and they get it wrong or you get people who miss it and -- sorry. And because of their attention deficit, like they don't see -- apologies, they don't see the stimulus and they miss it. So the software does give you that information, which you can interpret. So I don't know the answer to the other part of the question, but that's actually exactly what you get back from this is are they catching the signal and responding perfectly or are they responding too quickly and getting it wrong?

DR. GALEN: Thank you, Dr. McGough.

DR. JENSEN: Dr. Adams.

DR. ADAMS: Yes, some of the programs -- I'm probably most familiar with T.O.V.A., of the ones that were discussed in the summary, will also give you kind of how those rates of response change over different blocks of time over the course of the tests and you can look at whether that performance level is sustained in a consistent manner or not.

DR. JENSEN: Ms. Edwards, you had a question or a comment?

MS. EDWARDS: I do. I wonder, are the patients or their families informed of the lack of efficacy of these devices before they're charged, you know, before they take these tests?

DR. ADAMS: That's a great question. Actually, one of the notes that I had put into the document was -- so like one of the other --

(Audio feedback.)

DR. ADAMS: -- the IRB at our institution and I would love to see an informed consent process for assessments like this, but that's probably outside of the purview of the FDA's discussion today.

DR. JENSEN: Any other comments or questions?

DR. PENG: Yes, I do have a few comments. So actually -- mainly, is clinical diagnosis from three source: parents, school, and patient self and a friend. So those history (ph.) should be measured by treating physician. So this device, the reason the sensitivity and the specificity is low is because ADHD is a complex disease and oftentimes is a comorbidity with the other disease such as autism, Collet syndrome, anxiety, depression, learning disability, they can all coexist. So this, all of those device should be a tool for ADHD symptom test. It's not specifically for any disease, so that's the reason the specificity and the sensitivity is low. So my point is two reasons, because this disease so complex, it should be diagnoses from all of the resource reported childhood behavior from school, parents, and a child's friends or the child self. There's a test that is a child performance only, this is wide angle,

provide some information to aid follow the ADHD diagnosis. So the final diagnosis for ADHD is still based on the clinician's overall assessment. Yeah, that's all my comments.

DR. McGOUGH: Yeah, so --

DR. JENSEN: Dr. McGough.

DR. McGOUGH: Yeah. So yes, diagnosis of ADHD is properly made by having a certain number of clinically significant symptoms in multiple settings and those symptoms are normed. The reason we require six symptoms is that gets you to the 93rd percentile of your age group and that's very well established, and that is the gold standard. These tests get at some aspects of brain functioning in some of these people, but for all the reasons we've said it's not at all specific to this disorder.

So again, I think the FDA's labeling, they're not going to pull these things and people pay for them, but I think the caveats that the FDA has suggested are pretty much where they should be.

DR. PENG: Yeah, it's similar to the gold standard in U.S. psychology testing. Yeah, that is only a tool to assess, you know, cognition (ph.) of dementia, psychological disease, it's similar to that. But the device -- a child, another reason for child forward to 18 years old. So the -- from the device, it gives the child ages to take the test. If we allowed the child to take the -- psychology testing, the paper/pencil test, a child will not finish because the brain fatigue and the visual fatigue. So this is similar to that, for this kind of a device, just as a tool to aid in the diagnosis. Unfortunately, it is low sensitivity and specificity because ADHD can be a disease alone but oftentimes coexist with other psychiatric disease, as well.

DR. JENSEN: Thank you very much. Any other comments from the Panel?

Dr. Goodman.

DR. GOODMAN: Yeah, I have sort of another question about the psychometric

properties of these tests and I want to know about what is known about the sensitivity to change. So if the test shows that somebody has problems with reaction time or some other metrics on the test suggests they have problems with attention, if you repeat the test, assuming there's no problems with repeating it, there's no practice effects, will it show improvement with effective treatment?

DR. JENSEN: So the question is essentially can the device be used to actually watch progression of treatment?

DR. GOODMAN: Correct.

DR. McGOUGH: The FDA provided some data about this in the briefing materials, it's variable. Some of them are more medication sensitive than others. Probably if you isolated the group that had the problems to begin with, remember, that's only going to be half of your sample, you might show more effects. So this is always, at best, a secondary measure in any study that's done and there are incremental benefits, but it's not -- the much better way to assess responses is the kid sitting still at school and getting better grades or the parents stop fighting with each other over the kid. So there is maybe some benefit if you were in disabled range to begin with, but it's not hugely efficacious in that regard.

Heather, you may have another idea.

DR. ADAMS: No, I completely agree. I think that, you know, looking at how children's function changes in their everyday settings is, to me, the best indication as to whether a child is receiving benefit. I don't know if it's appropriate to think about these computerized tests as sort of the biomarker that's intermediary, but it's imprecise and maybe that's not the best to think of it, either. The other thing is if you give a child medication and then you bring them back into their clinic or some room to do this test for 15 minutes, that's a 15-minute snapshot of their day. That has to be done at a certain point of time based on the medication that they're taking and when that medication is peak in

their body and all the rest. But those ratings of the child's performance are going to capture how they're doing across a period of hours or days in multiple settings and that's going to be -- to me -- more useful in understanding whether the treatment is working and whether there are times of the day where you don't have the coverage for the medication, for example, or you have wear-off or -- I'm sort of rambling now but I'm just kind of expanding, I guess, on what Dr. McGough said.

DR. JENSEN: Thank you.

Dr. Cooper, you have a question?

DR. COOPER: Yes. Well, it goes back to the comment about the IRB. I mean, I think one of the things, we should be able to recommend that there be a careful review of the informed consent process when using these, especially about the efficacy and the confidentiality of information.

DR. JENSEN: Thank you.

Dr. Gupta.

MR. GUPTA: Yeah, I just wanted to add one comment related to Dr. Galen's question about sampling frequency, just to note that these products are -- that there is bench testing performed as part of the clearance process, as part of the 510(k) submission, in order to verify that the devices measure reaction time as accurately as possible and part of that is assessing sampling frequency.

DR. JENSEN: Thank you very much.

DR. COOPER: Thank you.

DR. JENSEN: So it looks like we have all of the questions answered. It may be time to go to the actual questions themselves. So thank you very much for that robust discussion. Let's focus our discussion now on the FDA questions. Copies of the questions can be found in your electronic documents and on the FDA website. I want to remind the

Panel, this is a deliberation period among the Panel members only. Our task at hand is to answer the FDA questions based on the data in the panel packs, the presentations, and the expertise around the table. Dr. Mohua Choudhury will now read FDA Question Number 1, there are three questions total.

Dr. Choudhury, please proceed.

DR. CHOUDHURY: Hi, everyone. Can you hear me okay?

DR. JENSEN: Yes.

DR. CHOUDHURY: Great. So for Question 1, FDA has identified the following risks to health for attention task performance recorders intended to (1) measure reaction time and associated patient performance in response to attention tasks only, and (2) aid in assessment or diagnosis of specific diseases or conditions.

Shown here are risks specific to the intended use category to measure reaction time and associated patient performance and response to attention tasks only.

And shown here are risks specific to the second intended use category, which is use to aid in assessment or diagnosis of specific diseases or conditions.

Given the identified risks to health, please comment on whether you agree with inclusion of all the risks in the overall risk assessment of attention task performance recorders under product code "LQD." In addition, please comment on whether you believe that any additional risks should be included in the overall risk assessment of these attention task performance recorders.

Do we stop here for discussion?

DR. JENSEN: Yes, I think we had discussed this already in our previous discussion. I'll just look and see if anybody has any of their hands up. I think I can summarize this. I think the Panel agrees with the inclusion of the risks in the overall risk assessment of these devices. Other risks that were of concern included the potential loss of confidentiality and

privacy, so we would recommend that there's the controls put into place to ensure that the data is confidential. The other risk that is of concern is one of financial burden and I guess that falls under a social type of risk, but it's a very real risk and so the question then becomes whether or not, in the use of these devices, informed consent should be required and that the parents and/or patient fully understands that, based upon the efficacy data, which is suspect, that they are assuming a potential financial risk to acquire data that may not be useful.

DR. ZHENG: Thank you, Dr. Jensen. All of the Panel members' recommendations are noted, we appreciate it very much. Thank you.

DR. JENSEN: You're welcome. Shall we go on to Question 2?

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

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

A device should be Class II if:

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

A device should be Class I if:

- general controls are sufficient to provide reasonable assurance of the safety

and effectiveness, OR

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

FDA 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 attention task performance recorders. Following are risk/mitigation tables which outline the identified risks to health for this device type and recommended controls to mitigate the identified risks, delineated by intended use.

Shown here are risks and corresponding mitigation measures specific to use to measure reaction time and the stated patient performance in response to attention tasks only, without aiding in assessment or diagnosis.

And shown here are risks and corresponding mitigation measures specific to use to aid in assessment or diagnosis of specific diseases or conditions.

a. Please discuss whether the identified special controls appropriately mitigate the identified risks to health for attention task performance recorders intended to measure reaction time and associated patient performance in response to attention tasks only, without aiding in assessment or diagnosis. This is the first

intended use category that was identified in previous slides. Please also discuss whether additional or different special controls are recommended.

DR. JENSEN: So can I go back to the ability -- are we going to do Questions 2a and 2b? Let's do them one at a -- well, actually -- I'm sorry, go ahead. Just go ahead and give us Question 2b.

DR. CHOUDHURY: Okay.

b. Please discuss whether the identified special controls appropriately mitigate the identified risks to health for attention task performance recorders in the second intended use category, which are intended to measure reaction time and associated patient performance in response to attention tasks for the aid in assessment or diagnosis of specific diseases or conditions. Please also discuss whether additional or different special controls are recommended.

DR. JENSEN: Okay, so can we now go back to the screen where I can see all the Panel members? And in addition to this question, I just want to go back to Question 1 for a moment, which you don't have to go back to, but to add a potential risk, there are Panel members that are concerned that given the nature of the tests it's possible that the patient may have a risk of induced epilepsy and whether or not that's a consideration under the potential risks that we need to address.

So okay, I think I have everybody up here now. Let's talk about whether or not the panelists believe that the special controls that have been identified by the FDA are appropriate for the device or was there any that they need to add. I'm just going to go around my little panel here and I'll start with Dr. Adams.

DR. ADAMS: In regards to whether these devices induce seizures in patients with epilepsy, I don't know that I have the data to answer that.

DR. JENSEN: So we're just going to add that, if it's possible, potential risk to list the

of potential risks that the companies -- the devices -- looking at what the risks are that may be identified with the devices. But in terms of -- so we're going about now the classification of the devices.

DR. ADAMS: Oh. Oh, okay.

DR. JENSEN: I'm sorry if I didn't make that clear. So the question is do you believe that the classification of Class II with the special controls that have been outlined --

DR. ADAMS: Yes, I agree.

DR. JENSEN: Dr. McGough.

DR. McGOUGH: I would agree, also.

DR. JENSEN: Dr. Johnston.

DR. JOHNSTON: I agree, Class II.

DR. JENSEN: Dr. Trumbower.

DR. TRUMBOWER: I agree, Class II.

DR. JENSEN: Dr. Goodman.

DR. GOODMAN: I agree, it should be classified as Class II and with the special controls, particularly labeling, which I think is quite important.

DR. JENSEN: Thank you.

Dr. McDavitt.

DR. McDAVITT: Yes, Class II.

DR. JENSEN: Dr. Lyden.

DR. LYDEN: Class II.

DR. JENSEN: Dr. Galen.

DR. GALEN: Yes, Class II.

DR. JENSEN: Dr. Ortiz.

DR. ORTIZ-AGUAYO: Class II.

DR. JENSEN: Dr. Kennedy.

DR. KENNEDY: Class II.

DR. JENSEN: Dr. Dorsey.

DR. DORSEY: Yes, agree to Class II.

DR. JENSEN: Dr. Anderson.

DR. ANDERSON: Yes, Class II.

DR. JENSEN: Dr. Cooper.

DR. COOPER: Yes, Class II.

DR. JENSEN: Dr. Pilitsis.

DR. PILITSIS: Yes, Class II.

DR. JENSEN: I think we've got everybody on the Panel now. So the recommendation of the Panel to the FDA is that this device remain -- be classified as Class II with the special controls, as outlined.

So the third question.

DR. CHOUDHURY: There is a third question, I'm just checking to see if folks want to have any additional discussion about special controls.

Lin, did you want to chime in?

DR. ZHENG: Yeah. Just we want to see if the panelists have any comment on our proposed special controls as written or if you have any additional suggestions for special controls that you would like the FDA to consider.

DR. JENSEN: Dr. Johnston.

DR. JOHNSTON: I may have missed it, but I did not hear what we discussed for a special control related to the privacy or breach of privacy issue, if they're in the cloud, that it is violated, so I would suggest that a special control for that be addressed.

DR. ZHENG: Okay, thank you. Yeah. And we -- that is something that the Agency

does review in terms of cybersecurity risk and sometimes that's reviewed as part of the software verification and validation, and at times we can also write an additional special control specific to the cybersecurity risk, dependent on how data is shared from the device, but we will definitely consider that, so thank you.

DR. JENSEN: Dr. Zheng, can the FDA also write a special control requiring informed consent?

DR. ZHENG: That is typically not something that we've done before. I'm not too sure and I can -- I'll invite our OHT 5 associate director for policy to chime in, as well, Mr. Sergio de del Castillo. Most of the time, for special controls, where we do have more regulatory oversight is to the labeling and if that is something that could be incorporated into the labeling, I think that's something where we would have more regulatory control over. But I'll turn to Sergio to see he has anything to add.

DR. JENSEN: Dr. de del Castillo.

MR. DE DEL CASTILLO: I'm not a doctor, but thank you. So I really don't have much to add, I was just going to point out that I don't know that we have the authority to require informed consent when a device is used, particularly if it's a prescription-use-only device, but we can rely on the labeling to provide additional information about the safety and effectiveness of the products, so we'll take that into consideration, as well.

DR. JENSEN: Thank you very much.

Can we go to our third question now?

DR. CHOUDHURY: Please discuss whether you agree with FDA's proposed classification of Class II with special controls for attention task performance recorders. If you do not agree with FDA's proposed classification, please provide your rationale for recommending a different classification.

DR. JENSEN: Thank you for that question.

I think as the previous discussion showed, that there was unanimous response from the Panel that Class II was an appropriate classification. Is that adequate?

DR. ZHENG: Yes. Thank you, Dr. Jensen and the panelists.

DR. JENSEN: You're very welcome. All right, so let's move on to the next device. Our second presentation today is by -- is from Ms. Kiyana Weatherspoon, who is now going to present on the optical contour sensing device.

Ms. Weatherspoon, please proceed.

MS. WEATHERSPOON: Good morning, my name is Kiyana Weatherspoon and I am a reviewer in the Division of Neuromodulation and Physical Medicine 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 the effort to classify optical contour sensing devices under product code LDK. These devices are currently unclassified and we are looking for your feedback and recommendation on the appropriate regulatory classification for these devices.

Here is the outline for today's presentation. We will begin the presentation by giving a brief device description followed by outlining the indications for use for these products, providing the regulatory history, clinical background, information related to the literature review, medical device reports, recall history, risks to health and mitigations, our proposed classification, and we will conclude with a couple of questions to the Panel.

Optical contour sensing devices are intended to measure various anatomical landmarks (for example, the spine or foot) for medical purposes. This could include monitoring and detection of musculoskeletal balance, posture and vertebral curvature or quantification of body angles related to postural asymmetries.

These devices may consist of an optical system which can be a camera or optical

scanner, for example. These products may also utilize sensors and software to allow for evaluation and assessment of these landmarks.

Most of the devices that have been cleared under product code LDK are over-the-counter devices, although some devices, such as the CryoVizion System, have been cleared for prescription use.

Representative indications for use for these devices include the following:

- To quantify angles on digital photograph depictions such as body angles related to postural asymmetries;
- To detect and monitor scoliosis;
- To screen and monitor scoliosis, lordosis and kyphosis;
- To provide topographical images to assist in the assessment of postural asymmetries;
- To evaluate musculoskeletal balance, posture and vertebral curvature; and
- To measure surface manifestations of the internal parameters of kyphosis, lordosis, and Cobb angle.

Optical contour sensing devices are a preamendments, unclassified device type. Preamendment devices are devices that were marketed prior to the Medical Device Amendments Act of 1976. These optical contour sensing devices are currently regulated through the 510(k) pathway and are cleared for marketing if found to be substantially equivalent to a legally marketed device. However, there's no regulation associated with the LDK product code because they are currently unclassified.

The following table includes the 510(k)s that have been cleared under the LDK product code. These include the CryoVizion System, Quantec Spinal Measurement System, Metricom, Terran Biomechanical Analysis System, the Integrated Shape Imaging System, and the Contourograph M-500.

Many of the devices noted on the previous slide are intended to detect and monitor scoliosis, kyphosis, and lordosis. As outlined in the clinical background of the Executive Summary, scoliosis is a lateral curvature of the spine that is greater than 10 degrees. Kyphosis is a forward curvature of the thoracic spine beyond the normal range of 30 to 50 degrees. Lordosis is a backwards curvature of the cervical and lumbar spine when viewed in the sagittal plane.

The etiology of scoliosis is not well understood and may arise due to genetic degenerative changes or an underlying medical condition, such as osteoporosis.

Management for this disease can be in the form of nonnarcotic pain medicine, various physical exercises, injection therapies, or surgical intervention. These management options are individualized and depend on the etiology, deformity, severity, and symptoms the patient is experiencing.

A literature search was conducted in order to assess information as it relates to safety and effectiveness of LDK products. An initial literature search was conducted in PubMed and Embase, which was limited to human studies that assessed safety or effectiveness of the cleared LDK products. These publications also had to be in English and not part of a systematic literature review. Unfortunately, this initial search did not yield any results related to safety or effectiveness of optical contour sensing devices.

Therefore, a second search was conducted using a time period from when devices were first cleared. However, this search also showed results unrelated to safety or effectiveness of optical contour sensing devices.

A third search was then conducted which focused on the specific brand names of the products that were 510(k) cleared. These were screened for the inclusion of the device name and whether they assessed device safety or effectiveness in scoliosis diagnosis. From this search, 10 relevant articles were identified and reviewed as part of this literature

review.

Most publications that were part of this literature review did not directly assess safety. However, given that these devices do not subject the users to radiation, these are generally recognized as low risk.

It was also acknowledged in the publications for this literature review that replacing X-ray with optical contour sensing devices for scoliosis diagnosis would lower the exposure to radiation.

During the literature review, a few publications argued that LDK devices should not replace X-rays for scoliosis diagnosis because there was evidence which suggested that some devices could be inaccurate. However, most of the publications reviewed favored optical contour sensing devices in place of X-rays for diagnosis of scoliosis.

In summary, it was concluded that optical contour sensing devices could replicate X-ray in diagnosis of scoliosis. Additionally, although most of the publications associated with this literature review did not assess safety, it was widely acknowledged that these devices minimize radiation exposure when compared to X-rays.

It is important to note that the literature review was limited. The first two systematic searches using the pre-specified terminology yielded no relevant publications, as the publications were not related to the assessment of the safety or effectiveness of optical contour sensing devices. Therefore, these conclusions are based on 10 relevant publications which focused on brand name specific searches on assessing safety and effectiveness in scoliosis diagnosis.

The next three slides provide background information for medical device reports, or MDRs. This information was summarized previously in the presentation for attention task performance recorders under product code LQD.

To further contribute to the benefit-risk assessment of optical contour sensing

devices, MDRs were reviewed. The Manufacturer and User Facility Device Experience, or MAUDE, was reviewed for the optical contour sensing devices cleared under product code LDK between April 1st, 1980 and December 31st, 2020. No MDRs were reported.

This slide provides background information for recalls in the medical device recall or MDR database. This information was summarized previously in the presentation for attention task performance recorders under product code LQD.

A review of the recall database found no recalls for devices under the LDK product code.

Although no risks were identified during the literature or MDR review, FDA identified the following probable risks to health based on the intended use and technological characteristics of optical contour sensing devices. Please note that we will ask for your input regarding the potential risks FDA has identified.

Given that some devices have been cleared to detect and monitor different conditions, the first risk identified is the risk of device failure or malfunction, which could lead to inaccurate results and diagnoses. If this were to occur, a user could potentially be improperly managed and have worsening of their condition.

The second risk identified was the risk of user error, which could lead to inaccurate results and diagnoses. If this were to occur, this could also lead to improper management or worsening of the patient's condition.

We propose that these risks will be sufficiently addressed by general controls and do not require special controls as part of the device regulation process.

This slide outlines our proposed regulation and classification for devices under the LDK product code given the intended use or risks that may result from device use. Devices under this product code will be identified as follows: An optical contour sensing device is intended for measuring various anatomical landmarks for medical purposes, such as to

detect abnormalities associated with postural asymmetry. The device may consist of optical system(s) such as a camera, optical scanner, or other optical unit, and may also utilize sensors and software for anatomical evaluation and assessment.

We also propose that these devices be classified as Class I exempt with general controls.

And with that, this concludes our presentation. Thank you for your time and attention. We do believe that your feedback is important and wish to gather your thoughts on the following questions.

DR. JENSEN: Thank you very much for that presentation. I want to open the floor to the experts around the table to begin deliberating on optical contour sensing devices, considering your expertise, everything you have read in the panel packs and heard in today's -- well, we didn't have anything in the Open Public Hearing, so from the presentations. So I want to open it up to our panelists.

It looks like Dr. Pilitsis has something to say, please start.

DR. PILITSIS: Thanks, Dr. Jensen.

So you know, I will say that I was -- I'm a neurosurgeon, I was a bit unaware of these devices until this panel discussion, so I did a quick Google search to see what they look like and basically, it's a camera that is able to use external landmarks to track scoliosis.

When you think about scoliosis X-rays, there's a huge amount of radiation and these patients are really frequently tracked, it's oftentimes children who we don't want to expose to radiation and again, it's like whole body films in different viewpoints and so this isn't just a chest X-ray once every 5 years, this is a big lift. And the idea that we can use this to be able to reduce that, you know, I'm not sure that I would say diagnose, which is one of my sticking points here, but definitely the hollowness, I think it's really low risk and even if you had a baseline and then to track that could be really helpful and I think it really adds value

with low risk to the patient. Thanks.

DR. JENSEN: Thank you very much.

Dr. Lyden.

DR. LYDEN: A question for the reviewers. I think I heard you say that most of these devices were over the counter and so my question is who actually uses them? Is this a device used in a medical office by a practitioner or by the parents? Who does the work?

DR. JENSEN: And to add to that, one of them was prescription and why was that one prescription? Dr. Weatherspoon? Or Ms. Weatherspoon.

MS. WEATHERSPOON: So the individuals that typically use these devices are medical professionals such as podiatrists, chiropractors and the like.

Vivek, do you want to comment on the most recent device being cleared for prescription use as opposed to over the counter?

DR. PINTO: Yeah. Actually, I don't have -- to answer that question, I'll have to look back, but also I would note there's multiple, I guess, uses here that we identified and found in our search. I do note that we had limited information in the literature, so we really relied on what we found in our internal records --

(Audio feedback.)

DR. PINTO: -- but it's not simply used for scoliosis monitoring --

DR. JENSEN: Well, so the literature that you gave us to review was all spine, yet it looked like there were indications for like the foot and some other things, so there's no data on that whatsoever, correct? On other body parts. It looks like all you had was spine. Dr. Pinto, am I correct on that?

DR. PINTO: Sorry, I thought Kiyana was answering.

MS. WEATHERSPOON: I believe that is correct because the first literature reviews that we were conducting, we had a bunch of different things to look at during that

literature review. However, the first literature review and the second literature review did not have any relevant articles that were related to safety and effectiveness of these devices. So the literature that focused on scoliosis diagnoses, in that we were able to find some literature related to safety and effectiveness of these devices.

DR. JENSEN: So I, like Dr. Pilitsis, had never heard of these, either, and when I went on line -- and it was really hard to find much on line also. But one of the things I noticed is that, as you noted in your review, they really sort of focused on these two companies, the Quantec, and there was the ISIS and the ISIS2, and just from the literature review for the Quantec, it's unlikely to supplant X-rays from a significant Cobb angle in one of the reviews. Another review, it mimicked X-ray in diagnosing mild scoliosis and then another review, it was reliable for monitoring it.

So I agree that it's really important to not irradiate these patients, but the question becomes whether or not these should be used to diagnosis scoliosis. Perhaps the diagnosis needs to be made the traditional way with X-rays, but would it actually be appropriate, more appropriate to use it to follow scoliosis so that you can eliminate those?

Dr. Kennedy, I see you have your hand up.

DR. KENNEDY: Yeah, so before I came to Vanderbilt, I was at Stanford, and my practice partners had a large scoliosis clinic in the Department of Orthopaedic Surgery there. These things are generally -- so I am familiar with them, they're the cottage industry of people that work on posture and they do a postural for a number of reasons. So these type of devices are generally used by that group, meaning whether it's a physical therapist or a chiropractor or even a non-medical person that is doing posture, they might come through and try to follow and show the patient what they're doing and how their posture is changing. They're generally not used by scoliosis surgeons for following, diagnosing, or doing -- while I completely get the desire to decrease radiation, we had many an instance

where people would come in and then say well, it's not that much changed on my posture analysis, here's my video of this, and then we take the scoli films, you're like yeah, well, you can compensate a lot with these. So they're not accurate enough to be used or to determine the need for surgery or surgical planning, which is what most physicians are using them for. I don't know if some of the bracing and some of that, I'm not aware of most people using it for that. If you're at a point bad enough to need it for bracing, you are -- for adolescents, you are generally followed with serial radiographs.

The real cottage industry, though, for this is not pediatric in screening and following that subset of patients, the real industry here is people that have a postural abnormality, whether it's fixed or not fixed, and they're getting some sort of treatment for it and they're being followed for it in that perspective. You know, there are people who come in with an increasing kyphosis where you don't need to follow it radiographically. You don't even need to follow it, you're just following it symptomatically, but people like to see that they're getting better with whatever treatment they're engaging in.

DR. JENSEN: Thank you very much.

DR. KENNEDY: That's generally what I have seen.

DR. JENSEN: So Dr. Tjoumakaris, do you have a comment?

DR. TJOUMAKARIS: Yes, thank you.

So I agree with Dr. Kennedy and Dr. Pilitsis. I'm a neurosurgeon out of Philadelphia and I don't think that these devices, from all the literature and the presentation, we haven't really established efficacy. I mean, they seem to be safe. But they shouldn't replace standard of care, especially from a surgeon's perspective. However, I agree with Dr. Pilitsis, there is a great concern, if a child is diagnosed at a young age, this is a lot of cumulative radiation in the spine, especially if it could be ordered from ancillary stuff, a therapist may order an X-ray and so on and so forth. So perhaps this should decrease the frequency of

monitoring X-rays, which you still have established in a diagnosis, get the proper Cobb angle if it ever requires surgery and then I'm not sure, you know, what standard of care in an asymptomatic patient is, whether it's every couple of years to get these X-rays, perhaps we can decrease that frequency but still maintain standard of care in between.

DR. JENSEN: Very good. Other comments, I guess, but because this has software involved with it, sort of harkening back to our first device that we talked about, a way to protect patient confidentiality, there's a risk any time -- obviously, you're using a software system that gets dumped into a database -- for loss of patient confidentiality, so that could, I guess, be a potential risk to include and make sure that the software is safe.

Any other individuals have anything to bring up? Any questions to ask the Panel?

(No response.)

DR. JENSEN: So I guess one question I have for the Panel, does anybody see a need for a special control with this device, since that would kick it up into a Class II?

(No response.)

DR. JENSEN: All right. So shall we then move on to the questions?

MS. WEATHERSPOON: Yes.

DR. JENSEN: Okay. So at this time let us focus our discussion on the FDA questions, and copies of the questions can be found in your electronic documents and on the FDA website. I want to remind the Panel this is a deliberation period among Panel members only. Our task at hand is to answer the FDA questions based on the data in the panel packs, the presentations, and the expertise around the table.

Ms. Kiyana Weatherspoon will now read the FDA question. There are two.

And Ms. Weatherspoon, please proceed.

MS. WEATHERSPOON: So FDA has identified the following risks to health for optical contour sensing devices:

- Device failure/malfunction leading to inaccurate results and diagnoses
- Use error leading to inaccurate results and diagnoses

Please comment on whether you agree with inclusion of all the risks in the overall risk assessment of optical contour sensing devices under product code "LDK." In addition, please comment on whether you believe that any additional risks should be included in the overall risk assessment of these optical contour sensing devices.

DR. JENSEN: Okay, so for our Panel, does anybody have anything to add besides the potential cybersecurity issues? You would agree with those risks?

(No response.)

DR. JENSEN: All right, so seeing the responses from the Panel, it looks like there are -- we would agree with the risks that you have indicated and would also include the risk of inappropriate data breach that would expose the patients' medical records, that that needs to be addressed.

And let's go on to the next question, please.

MS. WEATHERSPOON: Are you all able to see my screen?

DR. JENSEN: No.

MS. WEATHERSPOON: How about now?

DR. JENSEN: Yes.

MS. WEATHERSPOON: Okay, perfect. Section 513 of the Food, Drug, and Cosmetic Act states a device should be Class III if:

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

device presents a potential unreasonable risk of illness or injury.

A device should be Class II if:

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

A device should be Class I if:

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

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

Please discuss whether you agree with FDA's proposed classification of Class I with general controls for optical contour sensing devices under product code "LDK." If you do not agree with FDA's proposed classification, please provide your rationale for

recommending a different classification.

DR. JENSEN: Okay. So to the FDA, Dr. Pinto, in looking at the request for anybody wanting to add special controls, the Panel, no one on the Panel seemed to indicate that a special control is needed. Last chance for anyone on the Panel who wants to speak up.

(No response.)

DR. JENSEN: I don't see anything. So based upon that, then the Panel would agree with the FDA that classifying this device into Class I is appropriate. Does that answer your question?

DR. PINTO: Yes, thank you, Dr. Jensen and the panelists.

DR. JENSEN: You're welcome.

All right, so we have a third one to do. We're an hour, a little over an hour ahead of time. Would everybody like to press on and to go on to the third one? I see a whole lot of heads nodding. Very good, okay. So we're not going to break for lunch. Instead, we are going to move on to discuss the plunger-like joint manipulator. We will now hear from Ms. Kaitlin Olsen, who will present on plunger-like joint manipulators.

Ms. Olsen, please proceed.

MS. OLSEN: Good afternoon. My name is Kaitlin Olsen and I am a lead reviewer in the Division of Neuromodulation and Physical Medicine 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 plunger-like joint manipulators regulated under product code LXM. 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 my presentation today. These are the items that we will be

discussing.

Plunger-like joint manipulators are intended to be used by licensed chiropractors, medical doctors, and other licensed healthcare professionals, for the external analysis and adjustment of the spinal column and/or extremities.

Most cleared plunger-like joint manipulators are handheld electromechanical instruments, which are either AC or battery powered. The power generated charges a solenoid which then generates a thrust force delivered to the patient via a plunger attached to a metal stylus.

Other plunger-like joint manipulators are composed of an actuator or electronic control and position stand which contain a release mechanism preventing excessive pressure being applied to the patient.

For both handheld and free-standing devices, the patient is positioned on the table while the chiropractor positions the stylus against the desired region of vertebrae. Thrust force can be adjusted and controlled by either clutches, tension knobs, or adjusting the capacitor's voltage.

The indications for use or IFU statement identifies the condition and patient population for which a device should be appropriately used. Plunger-like joint manipulators are indicated for chiropractic adjustment, mobilization, or manipulation of the spine and/or extremities. Most IFU statements do not identify a specific disease or a condition to be treated, but almost all specify targeting specific vertebrae, ligaments, or soft tissue. Devices have been cleared for either over-the-counter or prescription use.

Plunger-like joint manipulators are a preamendment, unclassified device type. This means that this device type was marketed prior to the Medical Device Amendments 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 LXM product code.

To date, a total of 30 510(k)s have been cleared through the premarket notification 510(k) pathway under the plunger-like joint manipulator product code LXM. Please refer to Section 2 of the Executive Summary for a complete list of cleared devices under product code LXM.

Plunger-like joint manipulators are used for spinal manipulation, also referred to as spinal adjustment, which is a form of manual therapy involving the deliberate high-velocity, passive movement of a joint in the spine or periphery.

The goal of manipulation includes reducing symptoms, such as pain, through passive movement of the affected and surrounding areas.

Manipulation or adjustment can be considered an appropriate treatment for musculoskeletal pain in the neck, back, shoulders, and certain headache syndromes.

Acute and chronic musculoskeletal pain is the primary indication for plunger-like joint manipulators, which can result from various problems including strain, sprain, overuse, tendinopathies, and arthritis.

Alternative treatment options for musculoskeletal pain include:

- Manual manipulation
- Heating or cooling therapies
- Bracing
- Therapeutic exercise
- Topical analgesics
- Injection or local anesthetics
- Various oral medications

We conducted a literature review to identify any published information between April 27th, 2010 and December 31st, 2020, regarding the safety and effectiveness of plunger-like joint manipulators. Searches were limited to publications in English and excluded conference proceedings and abstracts.

A total of seven articles were selected for review based on their relevance to the reported safety and/or effectiveness of these devices. Of the seven articles, six reported randomized controlled trials, or RCTs, and one reported a prospective observational cohort study. I'll briefly summarize some of the take-home points for each of these review articles in the next few slides.

In terms of safety, three of five articles reported adverse events associated with the use of plunger-like joint manipulators when treating neck pain. The reported adverse events include:

- Pain
- Arm weakness and numbness
- Headache
- Fatigue
- Dizziness
- Stiffness, soreness, and pain during neck movement

No articles reported adverse events for treatment of low back pain.

Of the seven articles, four of the five studies reported statistically and/or clinically significant reduction in pain, while the remaining two studies did not provide statistically or clinically significant improvement in low back pain compared to manual manipulation or usual medical care.

In summation, minimal safety risks were reported in the literature with three of seven studies reporting mild and transient adverse events.

Five studies evaluated the effectiveness of plunger-like joint manipulators in the treatment of neck pain. Four of these studies reported statistically and/or clinically significant reduction in neck pain. The remaining two studies evaluated the effectiveness of plunger-like joint manipulators in the treatment of low back pain. These studies did not demonstrate statistically or clinically significant improvement in pain or disability outcomes compared to manual manipulation or usual medical care.

It should also be noted that the identified studies evaluated plunger-like joint manipulators for spinal manipulation only, even though these devices are also cleared for other uses such as extremity manipulation and mobilization.

The next three slides provide background information for medical device reports or MDRs. For the sake of time, I will not go through this information in detail since it was summarized previously in the presentation for attention task performance recorders under product code LQD.

To further contribute to the benefit-risk assessment of plunger-like joint manipulators, the Agency reviewed individual medical device reports, or MDRs, for this product code using the FDA's Manufacturer and User Facility Device Experience or MAUDE database. The Agency searched the MAUDE database to identify adverse events related to the use of plunger-like joint manipulators under product code LXM entered between April 1st, 1988 and December 31st, 2020.

The search identified five relevant MDRs. Of these five relevant MDRs, four MDRs were related to injury and one MDR reported malfunction. Of the four MDRs relating to injury, two reports noted an unspecified injury, one report noted pain and hearing loss, and one report noted pain, paralysis, and dyspnea. The malfunction report was a manufacturer report that noted failed repair of the device and no known patient involvement.

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 attention task performance recorders under product code LQD.

A review of the medical device recall database identified one Class II recall. A model 8000 Atlas C-1 orthogonal adjusting instrument was recalled in 2013 because the firm was marketing their device without marketing authorization.

To determine the appropriate classification for plunger-like joint manipulators, 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 used FDA's MAUDE database to identify MDRs and the information available to FDA regarding cleared devices. We also conducted the previously discussed literature review.

Here are the five risk categories we've identified for plunger-like joint manipulators:

Adverse tissue reaction. This can result from the use of device materials that are not biocompatible.

- Electrical shock or burn. This can result from electrical failure or malfunction.
- Pain. This could be due to a mechanical, electrical, or software malfunction causing device failure. Types of pain include neck pain, radiating pain, and mid-back pain.
- Discomfort. This can be caused by a mechanical, electrical, or software malfunction causing device failure. Types of discomfort include headache, fatigue, dizziness, stiffness, mild soreness, arm weakness, and arm numbness.
- Tissue injury. This could be due to a mechanical, electrical, or software malfunction causing device failure. An example of tissue injury includes bruising from excess force or pressure.

Here is a table with the identified risks and proposed mitigation measures which will be addressed through special controls. We believe general controls by themselves are insufficient to provide reasonable assurance of 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.

To mitigate the risk of adverse tissue reaction, we recommend biocompatibility evaluation.

To mitigate the risk of electrical shock or burn, we recommend electromagnetic compatibility or EMC testing and electrical, mechanical, and thermal safety testing.

To mitigate the risks of pain, discomfort, and tissue injury, we recommend EMC testing, electrical, mechanical, and thermal safety testing, nonclinical performance testing, software validation, verification, and hazard analysis and labeling controls.

Here is our proposed classification regulation for plunger-like joint manipulators. Part (a) of the regulation defines the device as follows: A plunger-like joint manipulator is an electromechanical device intended to perform chiropractic adjustment or manipulation of the spinal column and/or extremities. Joint manipulation is achieved through a thrust force delivered to the patient via a plunger attached to a metal stylus, positioned over the desired region of the vertebra.

Furthermore, we are proposing these devices 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 plunger-like joint manipulators under product code LXM:

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

2. Electromagnetic compatibility and electrical, mechanical, and thermal safety testing must be performed.
3. Nonclinical performance testing must characterize the thrust force applied to the patient.
4. Software verification, validation, and hazard analysis must be performed.
5. Labeling must include:
    (i) A warning that the device could cause pain, including neck pain, radiating pain, mid-back pain, and tissue injury.
    (ii) A warning that the device could cause discomfort, including headache, fatigue, dizziness, stiffness, mild soreness, arm weakness, and arm numbness.

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

DR. JENSEN: Thank you very much for your presentation.

I would like to open the floor to the experts around the table to begin deliberating on the plunger-like joint manipulator devices, considering everything you've read in your panel packs and from the presentations, and I'd like to start by saying is there anybody on the Panel that actually uses these devices? I went online trying to look at some -- find some pictures of them and some of them just look like handheld massagers. And so anybody who actually uses the device? Let's see, I've got three hands up, so let's go first to Dr. Trumbower.

DR. PINTO: Dr. Jensen, could I make one comment? I'm sorry to interrupt.

DR. JENSEN: Yes.

DR. PINTO: Yeah, so there was a statement in the Executive Summary and in the presentation that these devices were cleared for prescription and over-the-counter use. We did go back to look at our cleared devices and we confirmed that they're all for either

prescription use or they didn't specify and likely it's because we didn't incorporate indications for use for them until -- I can't remember the date, but it was sometime in the late '90s or early 2000s. But we believe that these are all intended to be used for prescription use only.

DR. JENSEN: Okay. And it sounded like they were to be used by licensed practitioners, it wasn't like they could write a prescription and the patient could take it home.

DR. PINTO: Yes.

DR. JENSEN: Okay. All right, so let's -- thank you very much, Dr. Pinto, for that clarification.

Dr. Trumbower, you had your hand up, let's start with you.

DR. TRUMBOWER: Yeah. My main point was related to the comment regarding over-the-counter use of this technology. The efficacy is just not strong at all and the potential for causing paralysis is a big concern of mine. Certainly there wasn't, to the best of my knowledge, any indication of whether or not there are limits to the doses with this technology and whether or not the paralysis or weakness may be permanent and in what ways do the studies indicate the potential source or target of the intervention and perhaps some of the symptoms, the negative symptoms, may be related to abnormal changes within the spinal cord itself.

So if they're applying different types of electromechanical perturbations to the spine, certainly if the spine is already compromised due to degenerative disease changes, narrowing of the cord, there's no reason to suggest that adding perturbations to that area could actually narrow the cord even further and result in a spinal cord injury and so that's a big concern. And I wouldn't necessarily think that if it is over the counter or if it's in a facility that they may be able to actually associate the two. So that's probably one of the

biggest concerns I have with this device and perhaps how the labeling for potential risks, especially with the risk being more on the subjective pain and discomfort, which seemed to be kind of the same in some ways, and related to the fact that it's device failure, I would say that it's not just the device failure that can contribute to these negative effects.

DR. JENSEN: Thank you very much. Yeah, the two complications concerned me, also. Unfortunately, there was not a lot of data about in what context those complications occurred. Looking at the studies, sometimes it wasn't -- the treatment wasn't just the device, it was the device plus manipulation. And the other complication that occurred, the one with hearing loss, made me very concerned that perhaps these patients actually had vertebral artery dissections and so they were throwing clots in the anterior and superior cerebellar artery, which could result in hearing loss, or they could take out PICO, which would definitely give them paralysis.

So there would be -- I have a lot of questions around those two cases. Do we have any more data specifically about the patients who clearly had neurological disturbance afterwards, because one of the things you don't mention in terms of tissue injury on your risks is one of actually vascular injuries, since the vertebral artery runs through the transverse processes of the cervical spine.

So to that point, Dr. Tjoumakaris has her hand up and I'll ask her to go ahead and make her comments.

DR. TJOUMAKARIS: Yes, thank you, Dr. Jensen. That's exactly my thought, I'm actually -- I'm a cerebrovascular neurosurgeon specialist and I have seen, at least once in my patients that I recall, patients that present with vertebral artery dissection. Unfortunately, these are not uncommon complications even with non-device chiropractic manipulation but unfortunately, there is this misconception that these devices are safer in manipulating and really, the concern is the -- cervical spine. And as you mentioned, the

vertebral dissection could be flow-limiting or could at least thrombo-embolize and lead to posterior circulation infarcts. Some could be as lucky as just having hearing loss or paresthesia. Others, unfortunately, can be life threatening and lead to vascular occlusion and thrombosis.

So I would agree that adding a warning for vascular injury with life-threatening complications is indicated and have major safety concerns before the device is approved for even physician prescriptions, let alone over the counter.

DR. JENSEN: Thank you for that. I agree entirely. Again, though, the question becomes was the patient manipulated in addition to the use of the device, because as those of us who treat these patients know, we've all seen patients who come in with chiropractic manipulation and with vertebral artery dissection, so that's a confounder. I hate to just say hey, it was due to the device but the patient was awesome.

Dr. McDavitt, you're next up.

DR. McDAVITT: Thanks. So there's a lot of people that practice manipulation and there's various grades of manipulation. I'm not endorsing the mechanical component, but I just want to talk about the risks and I mean, there's been lots of studies done on the risks of cervical high-rotation velocity vertebral artery damage, some not knowing if it was there beforehand and some not knowing it afterwards.

But I just would like to point out that the International Federation of Orthopaedic Manipulative Physical Therapists, an international organization, worldwide, it sets up a whole criteria on practice screening before providing these situations, so there are screening criteria available. There is a lot of controversy about whether or not the actual positioning of the test for screening people for these vertebral artery issues is actually worse than the manipulation procedures, so they have taken the approach of staying away from that as much as possible in order to do screening. So I guess, you know, we're not

going to talk about techniques because we're not supposed to point fingers and that's -- the issue is, is where should we classify it. And I agree, I think there should be conditions, but I'm concerned about using the term licensed because there are professions that -- licensed systems that have an associate's degree, physical therapy being one, chiropractic being another, that could be considered as licensed, but they're not qualified. So I think somehow if we're going to put a condition there that these people need to be trained, specifically trained in manipulation and do proper screening before using any type of device.

It's interesting to me that I noticed that what little studies were there, there were very little effects on the lumbar spine and more of the issues related to the cervical spine. Well, frankly, as someone practices -- therapy, these devices are so small, they'd be so subtle in terms of affecting larger joints, so probably there's more uses than that. But if you see how these are used, I mean, there are some practitioners using it on animals (ph.).

So I'm not going to go there, but I just wanted to mention that (a) I think there should be proper screening, like any other manipulation procedure, that that shouldn't be lost, and (b) we talk about people that are licensed; they should be qualified, not just licensed because that can be something that's sub-classification of license. So I'll stop there.

DR. JENSEN: But Dr. McDavitt, when you say proper screening of the patient, can you expand on that some?

DR. McDAVITT: Sure. It's a huge document, but let's just take some simple patient questionnaires, you know, dizziness issues, things that create peripheral extremity mobility types of things that might be considered similar to -- people talking about different changes in their hearing or when you screen the cranial nerves, looking for those responses, all those things that -- I mean, there's even a subtle -- there's a subtle "when in doubt, you

don't do it." And frankly, there's so many other procedures in manual therapy that can be done without a rotation that -- you know, the risk-benefit equation.

But the problem I think that Dr. Trumbower was talking about is when you're doing a manual therapy technique you're feeling responsiveness from the patient and you're screening as you're doing it. It's not just -- you just don't walk up and just do a procedure, there's whole steps forward to doing a procedure and when you have a mechanical device you lose all of that because now there's somebody between you and what you feel for tissue reactivity, tissue response, patient response, all of that's gone. So I would think that that would take a little bit more training and a little bit more responsiveness to think about. So I think you lose that control factor when you start messing with that. Maybe somebody else has something to say.

DR. JENSEN: Thank you very much for that.

Dr. Lyden, you're next.

DR. LYDEN: So Dr. Johnston and I come at this from the opposite end of the field, we receive the stroke patient after the event and the history of this goes back a long ways. Let me assert, first of all, that the instructions for use statements for all of these devices state they are intended for adjustment. So the fact that manipulation happened at the time of the use of the device, when the injuries occurred, is not a confounder, it's actually the intended use. So these devices are intended to be part of a spinal manipulation or a spinal adjustment. So that's what they're for. And reviewing each, every single one says intended for use as manipulation.

Now, manipulation has a history. Some of you have seen stroke patients, but I know I speak for Dr. Johnston when I say we see one every other month, maybe one every 3 months. It is not as common as it used to be, and the American Society of Chiropractors has stated in policy and in guideline documents that if manipulation is done correctly, it does

not pose a risk. So there's an area of uncertainty there, whether dissections occur as a result of improper technique or if it's an inherent risk of spinal manipulation with or without this mechanical device. And the typical outcome of the dissections that I see are significant neurological disability or death due to basilar occlusion.

So given the uncertainty, I think the only reasonable classification for this device is Class III because we just really don't have the data to know what the true incidence of death and stroke are after this device use and if I understand your briefing correctly, a Class III designation would then allow the device manufacturers the opportunity to file a PMA, which would enable all of us to look at more data, assemble the data, and think through really what is the risk of this device, what is the risk of this procedure, and what is the evidence that there's a benefit that outweighs the risk of stroke and death.

DR. JENSEN: Dr. Cooper.

(No response.)

DR. JENSEN: Dr. Cooper, you're still --

DR. COOPER: Yeah, sorry about that. It just took me a second to get the mute off.

So I agree, this is really -- I think this should be started as a Class III device. It's really a robot, a medical robot, even though it's a handheld medical robot or at least it should be treated that way, from my perspective, and that way we can be sure that people are properly trained to use it, people -- that there's sufficient safety mechanisms, feedback control mechanisms, and it's also sufficiently regulated because that's basically what it is, it's a handheld robot.

DR. JENSEN: Thank you very much.

Dr. Pilitsis, are you still on? Hi, let's have your thoughts on this, too, please.

DR. PILITSIS: You know, I heard everything that was said and I think that the vascular complications are, of course, really frightening. I do like the idea that was proposed by one

of the panelists in terms of making sure that this is somebody that is qualified to do manipulation and use this in conjunction with that -- I do -- and I thought the points about the lumbar and the cervical spine were interesting, as well. You know, while I have a great fear as a neurosurgeon about the cervical spine, I have less fear in terms of the lumbar spine. I get that it's probably not going to work as well there, but different sets of controls for those two things are probably appropriate.

DR. JENSEN: Thank you very much.

Anybody else? Dr. Dorsey.

DR. DORSEY: So can we make it contraindicated for use in the neck?

DR. JENSEN: To our FDA panelists, Dr. Pinto, can you answer that question?

DR. PINTO: Yeah. So for a contraindication, you can propose to, but it also works the same, as I understand, as an indication where you have to have the data to support that.

DR. DORSEY: Well, I think we have great data to support that. I see no evidence of efficacy at all. I think it's reasonable assurance of lack of effectiveness.

DR. PINTO: Yeah, I'm sorry. I was just trying to explain the --

DR. DORSEY: Yeah, yeah, yeah. And I think all we're hearing is significant -- I mean, we have -- so I don't think there's any question that this device has -- based on the evidence that we have to date, that there's more harm than benefit and that it should be contraindicated for use in the neck, and if the device needs to remain on the market because it is a preamendment device, then just having it for the lower back for Class III and have evidence to be brought forth to demonstrate its effectiveness for that indication would be reasonable.

DR. JENSEN: Yeah, Dr. Loftus.

DR. LOFTUS: Yeah, thank you, Dr. Jensen. Look, I know I'm here as the director, but

I have to talk clinically just for a second about this. I was just waiting for all of the vascular neurologists and vascular neurosurgeons to talk about this thing, I mean, this -- not necessarily with this device, but this is a common devastating problem that we all see and we've all been astounded by the level of denial in the chiropractic community when we see these things happen.

I will point out, you don't need to use a device to get a vertebral injury, they happen all the time in the absence of that just from various maneuvers including one that seems to be particularly suspect, called the toggle move, they're done on a drop table, and I just -- we've seen it over and over again and I just had to say it. Thank you.

DR. JENSEN: Dr. Johnston, you look like you want to say something.

DR. JOHNSTON: No, I'm in agreement with all of these comments about concern about vascular risk.

DR. JENSEN: And just looking at the data, you know, I went through the Executive Summary and all of the different trials, and although the FDA came up with there being an improvement in pain, there was really only one trial, which was that prospective, randomized, double-blinded, placebo-controlled trial of C5 instrumentation for shoulder pain, and that was really the only one where it was clearly the device application versus the placebo that actually showed statistically significant difference in the outcomes. The other ones, there was either a trend or it was never just the device, it was the device plus manipulation or muscle adjustment or whatever.

So in terms of efficacy, that was the only thing that I saw that actually seemed like it was -- it actually showed true efficacy. The rest of it, to me, it's very confounded by the fact that there are other maneuvers that are associated with use of the device. So that's kind of the struggle I have as to whether or not what we're being tasked with doing is looking at the device and what all the literature seems to be is looking at a procedure that is more than

just placement of the device on the area. So that's an issue for me. But I don't get a vote, I'm just the chairperson, so somebody -- anybody else want to have more conversation about this?

(No response.)

DR. JENSEN: Okay, so let's go to our questions, then. At this time we're going to focus our discussion on the FDA questions. Copies of the questions can be found in your electronic documents and on the FDA website. I want to remind the Panel, this is the deliberation period among the Panel members only. Our task at hand is to answer the FDA questions based on the data in the panel packs, the presentations, and the expertise around the table. Dr. Olsen will now read FDA Question Number 1. There's three of them.

MS. OLSEN: Can you all see my screen?

DR. JENSEN: Yes.

MS. OLSEN: Okay. FDA has identified the following risks to health for plunger-like joint manipulators:

- Adverse tissue reaction
- Electric shock or burn
- Pain
- Discomfort
- Tissue Injury

Please comment on whether you agree with inclusion of all the risks in the overall risk assessment of plunger-like joint manipulators under product code "LXM." In addition, please comment on whether you believe that any additional risks should be included in the overall risk assessment of these plunger-like joint manipulators.

DR. JENSEN: So I think, based upon the discussion, we agree with the risks that you include. However, there are other risks that need to be included and that would include

injury to the blood vessels, stroke, death, disability. And anybody on the Panel have another risk? Spinal cord injury and paralysis.

DR. LYDEN: To be evidence based for a second, the relationship between manipulation and vascular injury is solid. The damage to the spinal cord is a little bit weaker in my understanding of the literature. I'm not sure that is as substantiated as vascular injury.

DR. JENSEN: So I would say that you could have a vascular injury resulting in a stroke of the spinal cord which is then spinal cord injury, I think, are you -- you must be referring to traumatic injury, like the actual device causing trauma to the spinal cord directly, correct?

DR. LYDEN: Right, I'm not aware of that height, that level of causality being established in the literature the way it is for vascular injury.

DR. JENSEN: Right, thank you.

DR. TRUMBOWER: Just a quick comment. I think in many cases the spinal injuries are due to secondary injury to areas around the cord, so presumably it could be a pretty significant change from blood flow, it could be inflammatory response that can put pressure on the cord. So any of those things will lead to spinal cord injury.

DR. JENSEN: So there could be a potential, although it doesn't seem -- although we don't have any data as to the case where the patient did have paralysis, as to whether or not that was a vascular or a traumatic injury, at least paralysis could be included, and whether or not you want to go further to talk about it being direct injury to the spinal cord, it's a possibility but unsubstantiated, at least based upon the data that we have.

So anybody else have any other additional risks that they want to include?

DR. JOHNSTON: Can I just comment on that, Dr. Jensen? If we are concerned that spinal cord is too strong, can we still include paralysis as a potential risk because

obviously --

DR. JENSEN: Well, there was actually -- my take on it, we actually do have a complication that was paralysis and it's associated with the use of the device. Now, whether that was due to direct trauma or due to vascular injury --

DR. JOHNSTON: Exactly.

DR. JENSEN: -- who knows without more information?

DR. LOFTUS: Dr. Jensen.

DR. JENSEN: Yes, sir.

DR. LOFTUS: Just a question as to semantics. I can't comment as a Panel member, I know, but really, when you talk about vascular injuries or brain and brain stem injuries, it's really not the spinal cord. We talk about a vertebral injury, customarily what we've seen is it's either cerebella or brain stem injuries.

DR. JENSEN: This is true. If the anterior spinal artery comes off of that vessel, however, you can have upper cervical cord injury, but I'm just saying, at the angiography unit.

DR. LOFTUS: Of course. Thank you.

DR. JENSEN: Okay, so can we go on to Question 2, please? Have we adequately answered the FDA's question?

DR. PINTO: Yes, thank you.

DR. JENSEN: Let's go on to Question 2, please.

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

- insufficient information exists to determine that general controls are sufficient to provide reasonable assurance of its safety and effectiveness or that application of special controls would provide such assurance, AND

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

A device should be Class II if:

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

A device should be Class I if:

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

FDA 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 plunger-like joint manipulators. The following is a risk/mitigation table outlining the identified risks to health for this device type and the

recommended controls to mitigate the identified risks.

The identified risks to health include adverse tissue reaction, electric shock or burn, discomfort, and tissue injury and pain.

Please discuss whether the identified special controls for plunger-like joint manipulators appropriately mitigate the identified risks to health and whether additional or different special controls are recommended.

DR. JENSEN: So to our panelists, I think in terms of this question, the proposed special controls addition should include a warning that the device could cause all of the potential negative effects such as stroke, paralysis, death, that we talked before, that have been listed as complications with this device.

Can I have the whole Panel picture back up again, please? Thanks.

Does anybody else want to add a special -- another special control or see any additions to this list?

Dr. Dorsey.

DR. DORSEY: I think it should be contraindicated for use in the neck.

DR. JENSEN: Very good, thank you.

Yes, as Dr. Dorsey has indicated, that these devices should be contraindicated for cervical treatments. Anybody else?

(No response.)

DR. JENSEN: Okay, so let's go on to your third question, please.

MS. OLSEN: Please discuss whether you agree with FDA's proposed classification of Class II with special controls for plunger-like joint manipulators devices. If you do not agree with FDA's proposed classification, please provide your rationale for recommending a different classification.

DR. JENSEN: Okay, so if we could go back to the Panel again, let's go around the

room. I think we've had some robust discussion as to whether or not this should be a Class II device or a Class III device. Is everybody clear on the difference between the two? Anybody have any questions they want to ask about that?

(No response.)

DR. JENSEN: All right, so let's go ahead and start with Dr. Trumbower. Class I, Class II, or Class III?

DR. TRUMBOWER: Class III.

DR. JENSEN: Dr. Johnston.

DR. JOHNSTON: Class III.

DR. JENSEN: Dr. McDavitt.

DR. McDAVITT: Class III.

DR. JENSEN: Dr. Lyden.

DR. LYDEN: Class III.

DR. JENSEN: Dr. Galen.

DR. GALEN: Class III.

DR. JENSEN: Dr. Dorsey.

DR. DORSEY: Class III. One note, I think for future ones, I think it would be good to have more practitioners involved in this because left to our own devices, neurologists are really risk averse and will -- we err on the side of safety, but having others who are more familiar with the devices and the potential benefits would be helpful.

DR. JENSEN: Thank you very much for that clarification.

Dr. Kennedy.

DR. KENNEDY: Class III.

DR. JENSEN: Dr. Ortiz.

DR. ORTIZ-AGUAYO: Class III.

DR. JENSEN: Dr. McGough.

DR. McGOUGH: Class III.

DR. JENSEN: Dr. Goodman.

DR. GOODMAN: I think Class III, but at some point I'd like to understand the implications of whether that would effectively take these devices off the market, for example, what additional studies would the manufacturers have to perform. So I'm going with the Class III, but I don't understand the implications for marketing of the product.

DR. JENSEN: Dr. Pinto, could you outline what will be required of the Class III designation?

DR. PINTO: Yeah. Actually, I do want to reference the Panel to the introduction regulatory sheet, there is a specific section that outlines this and I can -- I mean, I don't want to just read it verbatim but actually, Sergio, you did such a great job yesterday describing that scenario and what would be required, could you chime in?

MR. DE DEL CASTILLO: So as we mentioned yesterday, the Day 1 Panel meeting, if the FDA agrees that this should be Class III and put out a final rule with that classification, the companies, the manufacturers of those devices, would have to submit a premarket approval or PMA application for our review. During that time, however, they are still permitted to legally market those devices, they would not be immediately taken off the market.

As part of the PMA, the company would be required to provide sufficient valid scientific evidence to demonstrate reasonable assurance of safety and effectiveness. If the PMA is not approved, meaning that we do not have sufficient evidence of reasonable assurance of safety and effectiveness, then the product would be considered misbranded and they would be required to remove it from the market.

DR. JENSEN: Thank you very much for that clarification.

Let's go back to our panelists. Okay, where did I end up? Dr. Goodman, did you vote?

DR. GOODMAN: Yeah, I did. I voted for a III and I asked the question about the locations for marketing.

DR. JENSEN: Sometimes the pictures make it rearranged and I forget where I am.

Dr. Pilitsis. You're muted. Yeah, you're muted.

DR. PILITSIS: Class III.

DR. JENSEN: Class III, okay.

Dr. Anderson.

DR. ANDERSON: Class III.

DR. JENSEN: Dr. Tjoumakaris.

DR. TJOUMAKARIS: Class III.

DR. JENSEN: So to the FDA panel, it's pretty clear that -- oh, Dr. Cooper.

DR. COOPER: Class III.

DR. JENSEN: Sorry. I'm sorry, I did not mean to skip you.

So to the FDA panel, to the FDA, it looks like the Panel unanimously agrees that this device should be a Class III device. From our discussion and the reason we came to this, the Panel came to this conclusion, is that there's clearly safety issues that -- with the device and that use of the device can lead to significant morbidity and potentially mortality, although there is no fatalities that were described in the literature.

To that end, the efficacy is suspect, too. It's clearly not there. For the lumbar spine and the cervical spine, there's very little data. So we have what's considered to be a significant safety issue with very little efficacy data and therefore the Panel feels that this should be classified as a Class III. Does that answer your questions?

DR. PINTO: Yes, it does. I was going to ask a further question, if you would consider

to propose a split classification based on the region, but I think you answered that, too, but if there's any further comment there.

DR. JENSEN: I think as Dr. Dorsey said, you could endorse it for the lumbar spine, but then there's no efficacy there. The two trials that you had were negative, so it doesn't really meet the efficacy here.

I would invite Mr. Wreh and Ms. Edwards to comment.

Mr. Wreh.

MR. WREH: Thank you, Dr. Jensen.

Well, I don't have anything to comment on, you know, my only concern is that we classified the device as Class III but, as the FDA say, it requires a PMA. So I think the manufacturer will be impacted by this presentation of their new product. So I'm not an expert in this field, so I would trust the judgment of the doctors to recommend it. Thank you.

DR. JENSEN: Ms. Edwards.

MS. EDWARDS: Hi. Well, I think you all have covered my concerns and I'm glad you changed it to level III because I was concerned and it's really scary to think about what could happen to a patient with someone who's not experienced in using that device, what they could do to a patient. So as a consumer, you all have -- yeah, your votes and your -- yeah, you have reflected my concern. Thank you.

DR. JENSEN: Thank you very much for your comments.

MR. WREH: Dr. Jensen, if you'll allow me to ask the FDA just one question, please.

DR. JENSEN: Yes, Mr. Wreh.

MR. WREH: Okay, so Dr. Vivek and I think, Lin. The question is Class I and 510(k) are the same, but they expect -- they are recommending Class III. Please explain why you're recommending Class I 510(k) exempt in the Executive Summary.

DR. JENSEN: So Mr. Wreh, I believe the FDA was recommending Class II because they had added special controls to the device.

MR. WREH: Okay, okay. I'm sorry. Okay, thank you.

DR. JENSEN: Um-hum.

MR. WREH: That answered my question. Thank you.

DR. JENSEN: Okay, so in summary of today's meeting, it looks like we looked at these three devices, the FDA Panel has agreed with the classifications of the first two devices and disagreed with the third. I think we've had discussion on that.

Does the FDA have any other questions for the Panel at this time?

DR. PINTO: No, we don't. Unless Chris, or Dr. Loftus, do you have any?

DR. LOFTUS: I'd like the privilege of making a closing comment, but that's just a gratitude comment. I can wait until you're ready.

DR. JENSEN: Well, so I was going to -- before I adjourn the Advisory Committee meeting, I was going to thank everybody, thanks to all the panelists and to our Industry Representative and our Consumer Representative for all of your contributions today.

And I would like to invite Dr. Loftus to make some closing remarks.

DR. LOFTUS: You're very kind, Dr. Jensen. Thank you.

I just want to express my gratitude to two groups of people, number one, the Panel members. This is a huge lift, two clinical days, two busy days you spent with us doing things that are very important for us to accomplish our mission, so the level of expertise that we've seen both days is, as it always is, just outstanding. The dialogue is outstanding among people from diverse backgrounds but very bright and very experienced and very talented and with the right motivations, so we're thankful for that.

And second, to the staff. I mean, you can see -- you don't see what goes on in the background, but everything you see on the slides, in the panel pack, have been gone over

and reviewed, I can't tell you how many levels of review to get ready for this. The staff is likewise an enormous lift, too, and the Panel, and just my gratitude to all of them. I wouldn't even single anybody out because so many of them -- and so much hard work, you can see it in what went on in these 2 days. So we thank you very much and we appreciate the efforts of our staff and it's been a very good session. Thank you.

DR. JENSEN: Yes, I really would like to echo that. The presentations were absolutely fantastic and you were really working so hard to give us the information that we need to make these decisions, and so thank you so much for your diligence in the presentations that you've done.

So these proceedings for the Neurological Devices Panel of the Medical Devices Advisory Committee meeting for June 3rd and 4th are concluded and we are now adjourned. Everybody have a great day.

(Whereupon, at 11:48 a.m., the meeting was adjourned.)

C E R T I F I C A T E

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

NEUROLOGICAL DEVICES PANEL

June 4, 2021

Via ZOOM Videoconference

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

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