UNITED STATES OF AMERICA

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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April 24, 2014
8:00 a.m.

Holiday Inn
2 Montgomery Village Avenue
Gaithersburg, Maryland

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DANIEL ARMSTRONG, Ph.D.	Temporary Non-Voting Member
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Concerned Citizen/Against device use

VITO ALVENESE
Concerned Citizen/Against device use

INDEX

INDEX

PAGE

INDEX

INDEX

M E E T I N G

(8:02 a.m.)

DR. YANG: Good morning. It is approximately 8:00 a.m., and I would like to call this meeting of the Orthopaedic and Rehabilitation Devices Panel [sic] to order.

I am Lynda Yang, the Chairperson of this Panel. I am a neurosurgeon at the University of Michigan, with expertise in spine, peripheral nerve, and brachial plexus surgery.

For today's agenda, the Panel will discuss current knowledge about the safety and effectiveness of aversive conditioning devices that are intended to deliver a noxious electrical stimulus to a patient to modify undesirable behavioral characteristics.

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

So, Dr. Reppas, why don't we start with you.

DR. REPPAS: Sure. John Reppas, M.D., Ph.D. I am the Director of Public Policy for the Neurotechnology Industry Organization.

MS. MATTIVI: Kris Mattivi. I am the Consumer Representative for the Panel. I am a physical therapist and a business consultant for Wellpoint.

DR. RICHARDSON: Donald Richardson. I am a neurosurgeon

specializing in functional neurosurgery at Tulane University Health Sciences Center.

DR. IWATA: Brian Iwata, Professor of Psychology, University of Florida.

DR. GREEN: Mark Green, Professor of Neurology, Anesthesiology, and Rehabilitation Medicine, and director of headache and pain medicine at Icahn School of Medicine in New York.

DR. WEIGLE: I'm Karen Weigle, and I am a clinical psychologist. I am affiliated with the University of New Hampshire's Institute on Disability, and I am a founder and clinician at the Chattanooga Autism Center.

DR. FOST: Norm Fost, Professor of Pediatrics and Bioethics at the University of Wisconsin, Madison.

DR. DORSEY: Ray Dorsey, Professor of Neurology, University of Rochester Medical Center.

DR. ARMSTRONG: Daniel Armstrong. I'm Professor of Pediatrics and Psychology and executive chair of PEDS and director of the Mailman Center at the University of Miami.

LCDR RUSSELL: Avena Russell, FDA/CDRH.

DR. BICKEL: Warren Bickel, Professor of Psychology, Virginia Tech.

DR. MILES: Steve Miles, Professor of Medicine and Bioethics at the University of Minnesota.

DR. GOODMAN: Wayne Goodman, Professor and Chair of Psychiatry at Mount Sinai in New York City.

MR. MIKITA: I'm Steve Mikita, Assistant Attorney General for the State of Utah. I represent the largest state agencies providing programs and protection for individuals with disabilities. I am a muscular atrophy patient representative.

Thank you.

DR. CONNOR: I'm Jason Connor, a biostatistician with Berry Consulting, and Assistant Professor of Medical Education at the University of Central Florida College of Medicine.

DR. AUGUSTINE: Erika Augustine, a pediatric neurologist from the University of Rochester, with expertise in clinical trials and developmental disorders.

DR. PEAVY: I'm Guerry Peavy, a research neuropsychologist in the Department of Neurosciences at the University of California, San Diego.

DR. STEBBINS: Glenn Stebbins, Professor of Neurological Sciences at Rush University in Chicago.

DR. KIM: Scott Kim from the NIH Clinical Center, Department of Bioethics. I'm also a psychiatrist.

DR. PEÑA: Carlos Peña, Division Director for the Division of Neurological and Physical Medicine Devices at CDRH.

DR. YANG: Thank you all for coming today and for bringing

your expertise to the table.

If you have not already done so, please sign in at the registration desk outside by the doors.

Avena Russell, the Designated Federal Officer for the Neurological Devices Panel, will make some introductory remarks.

LCDR RUSSELL: Good morning. I will now read the Conflict of Interest Statement, as this will become part of the federal record.

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 rep, 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. Code 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. Code 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 service outweighs his or her potential conflict of interest.

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

For today's agenda, the Panel will discuss current knowledge about the safety and effectiveness of aversive conditioning devices that are intended to deliver a noxious electric stimulus to a patient to modify undesirable behavioral characteristics. FDA is seeking clinical and scientific expert opinion on the risks and benefits of certain aversive conditioning devices based on available scientific data and information.

The Agency is considering whether to ban aversive conditioning devices that are intended to administer a noxious electric stimulus to a patient to modify undesirable characteristics. This meeting will concern only devices under 21 C.F.R. 882.5235. That includes all aversive conditioning devices (Class II) that are not self-administered. Devices that deliver a

noxious electric stimulus automatically are not considered to be self-administered devices.

Based on the agenda of 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. Code Section 208.

Dr. John Reppas is serving as the Industry Rep, acting on behalf of all related industry, and is employed by Neurotechnology Industry Organization.

We would like to remind Panel members and consultants that if the 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 participants to advise the Panel of any financial relationships that they may have with any firm at issue.

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

For the duration of the Neurological Devices Panel meeting on April 24th, 2014, Drs. Wayne Goodman, F. Daniel Armstrong, Warren Bickel, and Norman Fost have been appointed to serve as Temporary Non-Voting

Members, and Mr. J. Stephen Mikita has been appointed to serve as a Temporary Non-Voting Patient Representative.

For the record, the following individuals serve as consultants for the Advisory Committee in the Center for Drug Evaluation and Research. Dr. Goodman is a consultant to the Psychopharmacologic Drugs Advisory Committee. Dr. Armstrong is a consultant to the Oncologic Drugs Advisory Committee. Dr. Bickel is a consultant to the Drug Safety and Risk Management Advisory Committee. And Mr. Mikita is a consultant to the Peripheral and Central Nervous System Drugs Advisory Committee. Dr. Fost is a consultant to 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 materials to be considered at this meeting.

For the record, all special Government employees have undergone the customary conflict of interest review and have reviewed the materials to be considered for this meeting.

These appointments are authorized by Jill Warner, J.D., Acting Associate Commissioner for Special Medical Programs, on April 21st, 2014.

Just a few brief announcements before I turn it over to Dr. Yang.

Today's transcript will be available for purchase from Free State Court Reporting, Inc. The telephone number is (410) 974-0947.

Information on purchasing videos of today's meeting can be found at the FDA registration desk.

The press contact person for this meeting is Jennifer Rodriguez.

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

If you are presenting in the Open Public Hearing today and you have not previously registered with Ms. AnnMarie Williams at the registration desk, please make arrangements to do so.

In order to help the transcriptionist identify who is speaking, please be sure to identify yourself each and every time you speak. You may also be asked to spell your name.

And, finally, please silence your cell phones and any other electronic devices at this time. Thank you.

Dr. Yang.

DR. YANG: Thank you, Ms. Russell.

We will now hear the regulatory history of aversive conditioning devices by FDA's Dr. Kristen Bowsher, and then proceed to FDA's clinical and scientific presentation.

I would, however, like to remind public observers that while this meeting is open for public observation, public attendees may not

participate except at the specific request of the Panel Chair.

Dr. Bowsher.

DR. BOWSHER: Good morning, Panel members and members of the public. My name is Kristen Bowsher, and I am a biomedical and electrical engineer with the FDA's Office of Device Evaluation, and I will be providing introductory remarks to FDA's presentation today.

This slide lists the members of the multidisciplinary review team that have been involved in reviewing the issue before us and who have participated in the preparations for this Panel meeting.

This slide provides the outline for FDA's presentation. After my introductory remarks, Mr. Amatrudo will provide an overview of the banning standard. I will then provide you with the regulatory history of electrical stimulation devices, or ESDs, for aversive conditioning, along with an overview of the device technology.

I will then turn the podium over to Dr. Como to begin the FDA clinical and scientific presentation. Dr. Como will discuss the clinical background information regarding SIB and aggressive behavior. Dr. Park will then discuss the benefits and risks associated with ESDs for aversive conditioning for SIB and aggressive behavior, followed by Dr. Roth-Cline, who will present on the ethical considerations with a particular focus on issues related to clinical studies. I will then return to provide a brief summary of the presentation.

The purpose of today's meeting. Based on a comprehensive review of all available data and information, the FDA is concerned that ESDs for aversive conditioning intended to deliver a noxious electrical stimulus to modify undesirable behavioral characteristics in patients who exhibit self-injurious behavior, or SIB, and aggressive behavior may present a substantial and unreasonable risk of illness or injury. Therefore, FDA is considering banning these devices under Section 516 of the Food, Drug and Cosmetic Act.

We are here today to obtain scientific and clinical expert opinion on:

- the risks and benefits associated with other treatment options for this population;
- the risks and benefits of ESDs for aversive conditioning to modify undesirable behavioral characteristics in patients who exhibit SIB and aggressive behavior;
- whether ESDs for aversive conditioning present a substantial unreasonable risk of illness and injury;
- potential approaches to risk mitigation;
- the risks and benefits of applying the ban to devices currently in use by patients; and
- whether a clinical trial could be conducted to evaluate ESDs for aversive conditioning for the treatment of SIB and aggressive behavior.

Mr. Amatrudo will now discuss the FDA standard for banning.

MR. AMATRUDO: Good morning. I'm Vincent Amatrudo. I'm an attorney in FDA's Office of the Chief Counsel. I'm here to talk a little bit about the banning standard. As Ms. Bowsher said, we're here to get your scientific and medical expertise as it relates to these issues, but it may be useful to have some of this background.

Under the statute, FDA may ban a medical device for human use if it presents a substantial deception or an unreasonable and substantial risk of illness or injury. It's under Section 516 of the Federal Food, Drug and Cosmetic Act.

Bans must be imposed by regulation, which means notice and comment and rulemaking. So if we decide to move forward with the ban after this meeting, we would do a proposed rule, we would obtain public comment on that proposed rule, and then do a final rule, if we decide to move forward.

We are only focused on the unreasonable and substantial risk of illness or injury prong of the banning standard. We will not be discussing the deception prong of the standard today.

Our regulations and preambles to those regulations provide some additional guidance on what the standard means, the unreasonable and substantial risk of illness or injury. Our regulations at 21 C.F.R. 895.21(a) provide that, in evaluating whether the risk is substantial, we ask whether the

risk is important, material, or significant in relation to the device's benefit to the public health. In the preamble to the 895 regulations, it provides that we ask whether the risk is reasonable in light of the state of the art. And to be clear, actual proof of illness or injury is not required, as provided in the preamble as well as the legislative history to the Medical Device Amendments of 1976.

A banning determination must be made on all available data and information. This could include a variety of types of data and information, including data obtained under other statutory provisions, information supplied by manufacturers, and voluntarily submitted information.

And we may only ban a device if we determine that the risk of illness or injury cannot be corrected or eliminated by labeling. So, first, we look at whether the banning standard is met. If so, then we ask whether it can be corrected or eliminated by labeling. And if so, we would proceed to address the labeling issues. If it can't be corrected or eliminated by labeling, then we may proceed with a ban.

Just a little bit about the applicability of a potential ban to devices in distribution and use. We have the option of deciding only to apply the ban prospectively to new devices or to devices already in commercial distribution but not yet sold to the ultimate user or also to the ultimate user that may already be using the device, and the final banning regulation must

specify which of these options we choose. And we do have a question related to this issue that we will pose to you later.

I'm going to turn it back over to Ms. Bowsher to talk about the regulatory history and the device description.

DR. BOWSHER: Hi. My name again is Kristen Bowsher, and I now will be discussing the regulatory history and providing a description of ESDs for aversive conditioning.

Aversive conditioning devices were on the market prior to the passage of the Medical Device Amendments of May 28th, 1976. As such, these devices were included in FDA's original device classification efforts.

As discussed in the proposed rule for the original classification of these devices, the Neurological Devices Classification Panel identified the following risks to health associated with these devices: worsened psychological condition (that is, the patient's mental condition may become worse if aversive conditioning is administered incorrectly or if the patient is not carefully selected for this treatment); the risk of electrical shock or leakage current from the device could injure the patient; and the risk of patient injury if excessive current is used or if it is applied incorrectly.

The proposed rule also cited these four literature articles.

The original Neurological Device Classification Panel recommended that aversive conditioning devices be classified into Class II because the Panel believed that the electrical hazards associated with the use

of the device could be managed with performance standards. FDA concurred with the Panel's recommendation, and after receiving no comments on the proposed rule, the classification was finalized in 1979.

Aversive conditioning devices were identified in the classification regulation, 21 C.F.R. 882.5235, as an instrument used to administer an electrical shock or other noxious stimulus to a patient to modify undesirable behavioral characteristics.

As Class II devices, these devices currently are regulated under the premarket notification or 510(k) process. This requires that new or significantly modified devices being introduced into the U.S. market show that they are substantially equivalent to an existing legally marketed device of the same type, which we call a predicate device; that is, the 510(k) process involves a comparison of a new device to a predicate device, rather than having an independent demonstration of the new device's safety and effectiveness.

The first aversive conditioning device, the Farrall Instruments' Stimulator Sonic Control, or Whistle Stop, was cleared in 1976 using a device marketed prior to the Medical Device Amendments as a predicate device. It was cleared as an aid in modifying unacceptable behavior that is socially or physically injurious.

Three additional devices -- the Self-Injurious Behavior Inhibiting System, or the SIBIS; the SIBIS Remote Actuator; and the Graduated

Electronic Decelerator, or the GED -- were cleared for the indication to treat self-injurious behavior in patients that are usually diagnosed as autistic or intellectually disabled. Both the SIBIS and GED are specifically indicated to be used only in patients where other forms of therapy have been attempted and have failed.

To the best of FDA's knowledge, there is currently only one entity in the United States, the Judge Rotenberg Center in Massachusetts, that has recently manufactured and is currently using ESDs for aversive conditioning.

I will also note that two other devices were cleared under this device regulation, and they were cleared for use in smoking cessation and nail biting. However, the FDA is not seeking input from the Panel regarding these devices, because we believe they present fundamentally different patient populations with different potential risks and benefits that do not raise the same concerns.

I'll now give a general device description.

In general, the main components of these devices include an electric stimulus or shock generation module, cutaneous electrodes, and either a remote monitor module or an automatic mechanism to trigger a stimulus to be applied to the patient.

The stimulus generation module is carried by the patient via a waist or back pack, and the electrodes are attached to the patient's skin. The

remote monitor emits a radio signal that is uniquely coded to a specific generator module and is controlled by a trained practitioner who determines when it is appropriate to deliver an electrical shock to the patient.

An example of a device with an automatic trigger is the SIBIS device -- shown on the right -- in which an acceleration sensor module is placed in a headband worn by the patient. When the sensor detects a blow to the head that is sufficient enough, it triggers an electrical stimulus to be applied to the electrodes placed on the patient's body.

So the details of this and the next slide are hard to read, but the intent is not for you to read them but rather to point out that there are numerous factors that go into adequately describing the device characteristics of ESDs for aversive conditioning. The table provides a listing of the output stimulation specifications such as output current, voltage, frequency and others, the electrode sizes and types, and recommended stimulation locations. These factors are all important when evaluating the effect a shock has on a patient and a patient's perception of that shock.

This fact is important, and FDA has a question for the Panel regarding whether device mitigation, such as device technological restrictions, could mitigate potential risks associated with these devices.

This slide just continues the table from the previous slide and includes a cleared GED device. As stated in a previous slide, the FDA is aware of only one center in the U.S. using these devices. The center is currently

using devices, the model GED-3A and GED-4, that have been modified from the FDA-cleared device, and they have not received clearance or approval, in violation of the Food, Drug and Cosmetic Act.

While the output of the 3A is similar to that of the GED, the average output current of the GED-4 is reported, in an article by Israel and his colleagues in 2008, to be almost three times that of the FDA-cleared GED device. The ban that FDA is considering would apply to all ESDs for aversive conditioning, whether or not they are currently cleared by the FDA.

Determining the degree to which ESDs for aversive conditioning can cause certain levels of pain intensity and unpleasantness is challenging, and as shown on this slide, there are a variety of device characteristics that have been shown to affect perception of a given shock.

A primary variable for determining the perception of an electric shock is electric current which passes through the body. However, this current is dependent upon the voltage and the resistance of the path it follows through two points in the body. This relationship is known as Ohm's Law, which states that the current is equal to the voltage divided by the resistance.

We'll note that the skin resistance is dynamic and varies from person to person, from stimulation location to stimulation location, and from time to time. As an example, skin that is dry and calloused will offer a high resistance to electricity and pass less current than sweaty skin, which offers

low resistance and is an excellent conductor of electricity.

Other device characteristics that have also been shown to affect the perception of shock include pulse duration, shock duration, stimulus frequency and waveform, the type of electrodes, and the location of the electrodes. It has also been shown that repeated shocks over a short period of time do not have an expected habituation effect but rather can cause an increasing amount of pain with each successive shock.

It has also been demonstrated in healthy subjects that there is a large range of inter-subject variability with respect to the perception of equally applied shocks. Individual body chemistry and other factors can have a significant impact on how electric current affects an individual. Some people are highly sensitive to current, experiencing involuntary muscle contraction with shocks from static electricity, while others can draw large sparks from discharging static electricity and hardly even notice it.

The influence of anxiety on an experience of pain and other pain responses is still largely unclear, and the nature of the hypothesized mechanism by which anxiety can affect pain varies widely. Some studies and hypotheses imply that anxiety increases pain, while others imply that it decreases pain or does not change it at all.

Behavioral characteristics and personality traits have also been shown to affect shock perception in healthy individuals. For example, in a study by Duker and his colleagues in 1999, they found that the personality

factors of introversion and extroversion accounted for statistically significant differences in pain sensation ratings of shocks, with extroverts producing lower pain scores.

I'll note that the data presented above is based on studies of individuals without disabilities. It is important to note that although the peer-reviewed literature often reports that individuals with autistic spectrum disorder, or ASD, are insensitive to pain or have high pain threshold, this is has been challenged in a recent article by Allely and his colleagues in 2013, in which they propose that not all children with ASD expressed their pain in the same way as "the neurotypical child" would (that is, crying, moaning, seeking comfort, et cetera), which may lead to a misinterpretation by caregivers and medical professionals that patients are insensitive or to an incorrect belief that the child is not in pain.

It should also be noted that electrical stimuli have a uniqueness when it comes to how they are perceived by an individual as compared to other aversive stimuli; that is, stimulation applied to the same sensory location can give both a cutaneous sensation of intensity (that is, touch, prick, itch, sharp pain) and also an emotional or affective feeling of discomfort or unpleasantness, such as uncomfortable, intolerable, agonizing, or horrible.

In conclusion, determining the degree to which ESDs for aversive conditioning can cause certain levels of pain intensity and unpleasantness is very challenging, and there are a variety of device and

individual patient characteristics that have been shown to affect these perceptions.

I will now turn the podium over to Dr. Como, who will discuss the clinical background information regarding SIB and aggressive behavior.

DR. COMO: Good morning. My name is Peter Como, and I'm the neuropsychologist and clinical reviewer in the Division of Neurological and Physical Medicine Devices at FDA. I will be presenting a brief clinical background on self-injurious and aggressive behavior in persons with intellectual and developmental disorders.

This overview will include the clinical manifestations of SIB, aggressive behavior, putative etiologies of these behaviors, methods for assessing these behaviors, and an overview of treatment interventions.

Please note that the Panel will be asked to discuss whether they believe there are effective treatment alternatives to ESDs for aversive conditioning and, if so, will be asked to discuss the benefits of these treatments as compared to the risks.

There's a relatively high incidence of SIB/aggressive behavior in this population, and it occurs quite frequently. The estimates range from a low value of 2.6%, which was drawn from a community survey of over 2600 developmentally disabled individuals, to up to nearly 40% in a specific institutionalized patient population. More recently, MacLean and colleagues reported a 32% prevalence of SIB or aggressive behaviors in a

neurodevelopmental pediatric clinic sample.

Common self-injurious behaviors observed in this population and others include head banging, hand biting, skin picking, excessive scratching, and cutting. More serious self-injurious behaviors, which may result in significant morbidity and mortality, include eye gouging/eye poking with a risk of blindness; non-accidental injuries producing bleeding, protruding and broken bones; swallowing dangerous substances or objects, burning one's self; insertion of objects into body orifices; and genital mutilation.

With respect to aggression, any behavior can potentially be an aggressive act, which is generally defined as conduct due to intensity and/or frequency presents an imminent danger to the self or other persons and/or property.

The etiology of SIB/aggressive behavior in this patient population essentially remains unclear. Our review of the literature has suggested various biologic and behavioral etiologies.

Among the biological etiologies include a biochemical hypothesis, which includes things like release of beta endorphins or some impairment or dysfunction of the serotonergic neurotransmitter system. SIB and aggressive behavior have certainly been reported to be clinical features of seizures, notably seizure activity in the frontal and temporal lobes. A number of genetic disorders such as Fragile X, Lesch-Nyhan, Cornelia de

Lange, et cetera, these genetic disorders often present with SIB and aggressive behavior.

Another biological hypothesis has been that these behaviors are a result of either hyper- or hypo-arousal levels to either reduce or increase one's arousal. Others have suggested that SIB and aggressive behavior in these developmentally disabled persons may actually represent a response to pain, such as an ear infection, a migraine, or GI distress.

And, finally, there's a sensory hypothesis which suggests that these individuals have abnormal or low levels of physical stimulation.

The behavioral etiologies are based upon the principles of operant conditioning and therefore are learned behaviors that are maintained by various forms of reinforcement. Some of the behavioral hypotheses that we reviewed in the literature include the environmental hypothesis, in which these behaviors are shaped by various environmental contingencies or triggers, such as the need to escape a stressful situation.

The positive reinforcement hypothesis broadly falls into two classes. One is increased attention, such that the individual engages in SIB/aggressive behavior which results in increased attention, which is then positively reinforced by serving to produce social interactions that seldom may otherwise occur for these patients.

The other positive reinforcement hypothesis is that individuals engage in SIB or aggressive behavior to obtain desirable tangibles or

activities.

Continuing on with some of the behavioral hypotheses regarding the etiology is the negative reinforcement hypothesis, which suggests that SIB/aggressive behaviors are used as either escape or avoidance responses which are maintained by the delay, removal, or attenuation of unwanted activity by the individual. It's important to note that the highest rates of SIB/aggressive behavior are often displayed when the individual is encountering a very difficult task condition.

The self-stimulation hypothesis has been proposed to account for SIB behavior that occurs without environmental triggers and may be more common in institutionalized settings and possibly linked to the biological arousal hypothesis.

The communication hypothesis suggests that SIB and aggressive behavior may occur due to frustration associated with difficulties in either expressive and/or receptive language, notably when the individual is seeking attention or trying to obtain a desirable activity or tangible.

Several different methods for assessing SIB/aggressive behavior in this population have been reported in the literature. Among the more common methods are functional analysis, descriptive analysis, and the use of behavioral rating scales.

Functional analysis is the identification of the relationship between SIB/aggressive behavior and relevant antecedents and

consequences on an individual behavior.

Common descriptive analyses use direct observation of SIB/aggressive behavior in the natural environment and rely on the collection of quantitative data collection methods such as frequency counts, scatter plots, et cetera. Antecedent behavioral consequence observations are typically completed by parents, teachers, or residential staff and could be quantified as probabilities or percentages.

In addition, there are a number of behavioral rating scales, which are listed on your slide, to assess SIB and aggressive behavior in this patient population.

I will now turn to a discussion of the treatment of SIB and aggressive behavior in this patient population based on our literature review. Our review found that the treatment falls broadly into two categories: pharmacological and behavioral treatments. In addition, a number of other alternative and experimental treatments have been reported in the literature.

With regard to pharmacological treatments, several classes of drugs have been investigated, the majority of which involved off-label use of approved medications, with the exception of risperidone and aripiprazole, which are the only FDA-approved drugs to treat behaviors associated with autism, such as irritability, aggressive behavior, SIB, and temper tantrums.

For this presentation, we are providing a comprehensive review of all pharmacological studies, including the off-label use of medications

which FDA considers as investigational or practice of medicine. Regulatory concerns regarding the off-label use of these drugs are addressed by our sister center at FDA, the Center for Drug Evaluation and Research, or CDER.

The majority of the pharmacological studies reported in the literature are limited by the use of single case studies or small case series designs, which employed a variety of outcome measures for assessing SIB or aggressive behavior.

However, there was a recent Cochrane Review that identified five randomized controlled trials in adults with intellectual disabilities, which included four trials of opiate antagonists and one trial of clomipramine.

Pharmacological treatments may reduce SIB/aggressive behavior if based on a putative biologic mechanism, for example, dysfunctional serotonergic reuptake.

The adverse event profile of these drugs that have been reported to treat SIB/aggressive behavior appears to be similar to that for the patient populations for which these drugs are indicated. Importantly, these pharmacological treatments have the potential to cause serious adverse events. A listing of the potential serious adverse events for these drugs are detailed in the Executive Summary.

The literature suggests that individuals with developmental and intellectual disabilities do not appear to be at a higher risk for developing AEs associated with these pharmacologic treatments.

With regard to specific pharmacologic treatments that have been reported in the literature, these include the use of typical and atypical antipsychotics. Risperidone has been the most widely studied with the major effects being reported on irritability and aggression, with less reported efficacy for self-injurious behavior.

A number of antidepressant agents have also been investigated, among these selective serotonin reuptake inhibitors, or SSRIs. They improve stereotypic and obsessive life behavior associated with self-injury and aggression. As I mentioned, a randomized trial of clomipramine, which is not a pure SSRI, demonstrated clinically significant improvement in the rate and intensity of SIB and stereotypy.

Opiate antagonists have also been widely investigated. As I mentioned, the Cochrane report identified four randomized controlled trials of naltrexone versus placebo, with a relatively modest reduction -- about 30% -- in SIB/aggressive behavior. The effects noted were largely for the short term, and the report suggests that these agents may actually worsen SIB or aggressive behavior in the long term, increasing the relapse rate if discontinued.

Additional pharmacologic treatments that have been reported in the literature include the use of mood stabilizers such as lithium. These have been largely limited to single case reports, and the use of lithium has been primarily used to augment the SSRIs. A number of anticonvulsant

agents have also been reported in the literature, which essentially have yielded equivocal results in reducing these behaviors.

Alpha agonists have also been used primarily to treat irritability in children with autism. The clinical effect, if any, may be due to the sedating effect of these drugs.

Other pharmacological interventions that have been reported in the literature include amantadine, which was a small randomized trial of 39 autistic children with irritability and aggression. However, there was only a 47% versus 37% reduction (drug versus placebo) in this trial. Ammonia, which is not a prescription drug, has been used primarily as an aversive treatment. The studies of ammonia are relatively older studies and limited to single case reports, but all report a benefit in reducing SIB.

Turning to behavioral treatment. Behavioral treatment is the most common approach. Several approaches to treat SIB/aggressive behavior in this patient population have been reported in the literature. Behavioral intervention is largely based upon the concept that SIB/aggressive behavior are learned behaviors and therefore responsive to environmental modifications.

Kahng and colleagues in 2002 did a quantitative analysis of the behavioral treatment of SIB over the period from 1964 to 2000. They identified 396 articles involving over 706 participants. Their analysis reported a mean outcome of all reported behavioral treatments, of an 83.7% reduction

in self-injurious behavior from baseline to the end of treatment. The authors concluded that the use of reinforcement-based treatments have increased in the past decade, whereas punishment-based treatments have decreased. These authors also suggested that early and effective intervention is essential to impact behavioral change and that greater emphasis should be placed on prevention.

There are a wide variety of behavioral approaches reported in the literature. The reinforcement-based treatments are listed on this slide. Specific details regarding these reinforcement-based treatments are provided in the Executive Summary.

Extinction-based treatments involve no longer providing reinforcement for a response that was previously reinforced, such as removing the individual from a setting when they engage in an SIB or aggressive behavioral act. This actually inadvertently maintains this behavior.

Another form of an extinction-based treatment involves the use of protective equipment, such as gloves, helmets, face shields, which prevent the individuals from carrying out the behaviors.

Although we typically do not think of adverse events being associated with non-pharmacologic intervention, a potential adverse event that has been reported to be associated with extinction treatment is the so-called occurrence of extinction bursts, which is an escalation of SIB or aggressive behavior, which is often common during the early phase of an

extinction-based treatment.

Additional behavioral approaches include punishment-based treatments. These include the presentation of an aversive stimulus, which can range from an electric shock, a water mist spray, the use of bitter substances, ammonia, or facial screening, or the removal of a positive reward when the individual engages in an self-injurious behavior or aggressive act.

Minshawi suggested that punishment-based treatments may be necessary to gain control over serious or dangerous SIB/aggressive behaviors when other treatments have failed. She also noted that the punishing stimuli or event must be strong enough to override that which is maintaining the behavior.

Another behavioral approach is the use of functional communication training, in which socially appropriate communication behavior is taught to replace less appropriate behavior. This allows the individual to regulate the delivery of the reinforcer, thereby exerting more control over their environment, but as you might imagine, it requires a relatively higher level of intellectual and cognitive function in order to engage in this type of therapy.

Other treatments that have been reported in the literature include the use of physical restraint that is not being used as a punitive measure and may be necessary to prevent serious or dangerous SIB/aggressive behavior to the self or others. It essentially relies on

immobilizing the individual via various forms of restraint, such as the use of wrist cuffs, arm sleeves, and four-point restraints.

Sensory integration training is based upon the theory that sensory dysfunction contributes to SIB and aggressive behavior. Therefore, the goal of this treatment is the stimulation of so-called neural processes involved in receiving, modulating, and integrating sensory input. An example of SIT technique is the use of a weighted vest.

There are a number of alternative treatments that have been reported in the literature. Many of these studies are older studies but include the use of techniques such as mindfulness training, which basically relies on meditation techniques; the use of contingent exercise, in which the individual has to engage in a brief physical exercise immediately upon committing a self-injurious behavior or aggressive act; the use of muscle relaxation, which is limited by the decreased intellectual capacity to understand and carry out instructions, especially in populations that have severe intellectual limitations; and, finally, there is the report of the use of a so-called Snoezelen room, which essentially is a multi-modal sensory environment type of room, in which a number of sensory and tactile and other types of stimuli are presented continuously, and it provides sort of a relaxing, peaceful type of environment.

There are a number of experimental treatments that have been reported in the literature, and these include the use of surgical techniques

such as ablative procedures, including amygdalotomy, limbic leucotomy, cingulotomy, and anterior capsulotomy. In addition, deep brain stimulation has been used -- has been reported in the literature. Please note, though, that DBS is not FDA approved for the treatment of SIB/aggressive behavior. However, the reported studies have largely targeted the posterior hypothalamus, both bilaterally and unilaterally.

The surgical studies are largely, again, single case reports, but all report a reduction in SIB/aggressive behavior, and none of these studies report the occurrence of any serious adverse events.

Electroconvulsive therapy, or ECT, has also been reported. Please note that ECT is not FDA approved for SIB/aggressive behavior. However, we did find a single case report of an autistic boy with bipolar disease and SIB/aggressive behavior who had a positive response to the use of ECT.

As noted in the regulatory overview by Dr. Bowsher, the general indication for electrical stimulation devices for aversive conditioning states that these devices are to be used only in patients where other forms of therapy have been attempted and failed. However, there does not appear to be any data or criteria available for determining treatment failure in this patient population. Thus, it's not clear when aversive therapy should actually be administered.

Some of the challenges for identifying treatment failure in this

patient population include that it is not clear how many other non-aversive treatments must be tried first. This is particularly salient if a careful functional assessment has not been completed to identify the target behaviors and the antecedents of the behavior.

As noted in the overview of treatments, there are a considerable number of pharmacological, behavioral, and alternative and experimental treatments, either alone or in combination, that have all been reported to be beneficial in reducing SIB and aggressive behavior in this patient population.

It's also not clear how long these treatments should last. It's possible that a beneficial effect of treatment may not occur acutely and only start to show some effect after a relatively long trial period. However, the length of treatment is not clear.

There's also a lack of a definition of intolerance, such as the occurrence of adverse events which would lead to a discontinuation of treatment.

And, finally, there's really a lack of a gold standard or objective criteria for determining response to therapy.

In summary, SIB/aggressive behavior are common comorbid behavioral conditions in individuals with intellectual and developmental disabilities.

The etiology of SIB/aggressive behavior in this patient

population remains unclear and includes biological and behavioral theories.

Careful assessment of SIB/aggressive behavior in this population assists in the targeting of appropriate treatment.

There are no current published consensus guidelines or practice parameters for the treatment of SIB/aggressive behavior.

Studies of safety and efficacy of treatments for SIB/aggressive behavior are limited by the lack of controlled trials and the reliance on single case reports or small open-label case series.

The treatment of SIB/aggressive behavior consists primarily of behavioral and pharmacologic interventions. Most interventions appear beneficial in reducing, but not eliminating, these behaviors.

Our review of the literature suggests that behavioral approaches should be used as the initial treatment. However, no specific type of behavioral treatment has emerged as a first-line treatment.

Pharmacological interventions may be more effective when combined with behavioral treatment.

Reporting of adverse events has been largely limited to the pharmacologic studies. However, the AE profile of drugs used to treat SIB/aggressive behavior in individuals with intellectual and developmental disabilities appear to be similar for that for the approved use patient populations. Moreover, there does not appear to be a higher risk of developing AEs in this specific patient population.

As I noted, adverse events can occur with some behavioral therapies, notably with extinction treatment and punishment-based treatments.

There is a lack of available data for defining treatment failure in this patient population.

So I'll remind the Panel again that the Panel will be asked to discuss whether they believe there are effective treatment alternatives to electrical stimulation devices for aversive conditioning and, if so, will be asked to discuss the benefits of these treatments as compared to the risks.

This concludes my presentation on the clinical background of SIB/aggressive behavior in this patient population. Dr. Lawrence Park will now present the benefits and risks associated with electrical stimulation devices used for aversive conditioning.

DR. PARK: Good morning. My name is Lawrence Park. I'm a psychiatrist at the Division of Neurological and Physical Medicine Devices at the FDA. I will present information pertaining to the risk/benefit assessment of electrical stimulation devices, or ESDs, for aversive conditioning.

According to the Food, Drug and Cosmetic Act, the FDA is required to consider all available data and information in making a banning determination.

Sources of information for the benefit/risk assessment include two systematic literature reviews to identify the benefits and the risks

associated with the use of ESDs for aversive conditioning. The benefit literature review focused on the indications "SIB" and "aggressive behavior." The risks literature review examined ESD use for aversive conditioning across all indications. The risks review was not limited to SIB and aggressive behavior because of the possibility that the risks of ESD use might not be indication specific.

In addition to the literature reviews, other sources of information considered in this review include:

- the Manufacturer and User Facility Device Experience, or MAUDE, database for medical devices kept at the Center for Devices and Radiological Health;
- reviews and reports submitted to FDA from independent sources, including recommendations and/or consensus statements from two professional or scientific organizations;
- prior public proceedings and governmental reports regarding ESDs for aversive conditioning;
- information from manufacturers;
- clinical interviews conducted by FDA staff with individuals who received ESD administration;
- parental reports and case reports submitted to the FDA by the Judge Rotenberg Center Parents Association; and

- other publicly available information.

Separate searches were undertaken for the treatment effect and adverse events associated with ESDs for aversive conditioning. Queried databases included EMBASE, MEDLINE, and PsycINFO. Search results were limited to English and human. A detailed description of the search strategies and search terms is presented in Section 5.1.1 of the Executive Summary.

Title and abstract review was independently conducted for each search by two review team members, and potentially relevant articles were obtained. These articles were then reviewed for inclusion.

In addition to the systematic searches of the databases, other potentially relevant articles were identified from other sources, including information submitted to FDA, prior public proceedings on the subject, and bibliographies of articles identified in the original search strategy.

Overall, the search yielded 57 articles (45 clinical reports and 12 reviews) regarding treatment outcome, and 39 articles (27 clinical reports and 12 reviews) regarding adverse events.

The 45 clinical reports identified in the systematic literature review of benefits included one case-control study conducted outside the U.S., one within-subjects comparison trial conducted outside the U.S., one retrospective review of 60 patient charts conducted in the U.S., one questionnaire follow-up study of 22 subjects with 11 respondents who received ESDs for aversive conditioning conducted in the U.S., and 41 case

reports or case series. No prospective, randomized controlled trials were identified.

The highest-quality publication was a case-control study of eight subjects with SIB compared to eight matched controls conducted by Duker and Seys in the Netherlands in 2000. They examined the use of the HSP 3012, a device not cleared in the U.S. The primary outcome measure was the difference in an author-determined mechanical restraint score after ESD administration in the active group. With device application, the ESD group had a significantly lower mean restraint score than matched controls.

Additionally, the authors reported that 82% of all subjects who received ESD administration had beneficial results over an up-to-eight-year period.

The authors reported a few problems that might interfere during the often-extended course of treatment, including individuals may adapt to the intensity of the electrical stimulus, self-restraint may emerge or may intensify, and individuals may show SIB at low intensities that eventually result in tissue damage, et cetera.

Limitations of this study include the fact that the primary outcome measure did not directly examine SIB, the unclear relationship between the mechanical restraint score and SIB, and the small sample size of the study.

The other comparative report was a within-subjects

investigation of heart rate at baseline and with the ESD applied. Duker and Van der Munckhof in 2007 examined the heart rate of five individuals being treated with severe SIB with ESD administration. They noted that when individuals were wearing an active ESD, their heart rate was significantly lower than when they were not. From this data, they concluded that individuals were less anxious when an active device was applied.

Limitations of this study are that heart rate has not been demonstrated to be a valid marker of anxiety, the association of heart rate or anxiety with SIB has not been established, and the small sample size of the study.

Israel and colleagues in 2008 conducted a retrospective chart review of 60 patient charts at the Judge Rotenberg Center, a special needs residential educational facility in Canton, Massachusetts. The review included individuals who had received ESD for aversive conditioning as part of their treatment program. They report the use of two different devices, the GED-1 and GED-4. They concluded that ESD use as a supplement to positive programming was effective, with effectiveness defined as a 90% or greater reduction of SIB or aggressive behavior from baseline in 100% of patients.

Limitations of this report include the retrospective nature of the review; methodological considerations, including the use of concurrent treatments and lack of statistical analyses; the unclear status of the journal in which the article was published -- the *Journal of Behavior Analysis of Offender*

and Victim Treatment and Prevention is an open-source, online electronic journal that has published six volumes since 2008. The ISSN number is pending and the use of a peer review process is unclear; finally, at least some of the authors have an unreported conflict of interest. The lead author was the executive director of the JRC, the manufacturer of the devices reviewed in the articles, and this relationship may represent a potential source of bias.

Murphy and Wilson in 1980 conducted a follow-up questionnaire study of subjects who had previously received ESDs for aversive conditioning. They sent questionnaires to 22 identified subjects and received 11 responses. Reviewing the responses, they found that relapse, defined as a marked increase in self-injurious behavior after treatment ended, occurred in 7 of 11 successfully treated patients within two years after treatment ended. Two subjects showed continued suppression of SIB symptoms.

Limitations of this study include the use of a questionnaire assessment with no direct interview or assessment of subjects, lack of statistical analyses, and small sample size with only 50% of queried subjects responding to the questionnaire.

Forty-one case reports and case series, encompassing 105 subjects, containing specific clinical report information on ESDs for aversive conditioning for SIB and aggressive behavior were identified. These articles are listed in Table 3 of the Executive Summary.

Review of the case reports and case series demonstrated a

short-term improvement, defined as during the time the device is actually applied for SIB and aggressive behavior. Sixty-six individuals had an immediate reduction in SIB and/or aggressive behavior, 10 had partial reduction, and 3 reported no benefit.

With continued device application, 23 individuals demonstrated continued reduction of symptoms, with 12 of those lasting longer than six months; 6 experienced relapse of symptoms, and 2 reported equivocal results.

When the device use was tapered off or faded off, three had continued reduction in SIB or aggressive behavior, while three experienced relapse of symptoms.

Limitations of this review, in addition to the non-prospective, non-comparative nature of the reports, include the use of different devices, the different usage of the devices, different stimulation parameters, varying duration of use and evaluation of the primary endpoint, lack of systematic evaluation of endpoints, and the variable use of concurrent treatments.

Though not systematically investigated, some researchers have theorized that magnitude and duration of effective ESDs may be dose dependent. One study by Williams, Kirkpatrick-Sanchez, and Iwata noted that the initial rate of reduction and the overall duration of reduction may be related to stimulus intensity.

Another study by Duker and Seys demonstrated reductions of

SIB up to eight years and concluded the loss of SIB reduction in other previous reports may have been due to the use of lower stimulation levels.

These findings suggest that effectiveness and duration of effect may be dose dependent; that is, higher intensity stimulation is associated with greater effectiveness and longer duration of effect.

Twelve review articles -- that is, articles not containing new clinical information -- examined the potential benefits of ESDs for aversive conditioning. These reviews generally supported the conclusion that ESDs for aversive conditioning for SIB and aggressive behavior demonstrate short-term reduction in those symptoms.

One review by Lichstein and Schreibman in 1976, of ESDs in autistic children, noted that in all of these studies, electric shock proved to be a highly effective therapeutic agent with autistic children and estimated that positive effects compared to negative effects occurred at a ratio of 5:1. However, they also reported that the lack of long-term durability, as well as setting specificity of results, may be an obstacle to overall satisfactory effect.

Four reviews examined longer-term effectiveness. One of them, Lernan and Vorndran in 2002, concluded that ESD use may have long-term effectiveness, while another, Logan and Turnage in '75, noted that the effect appeared to be short term only, that is, symptoms are only momentarily suppressed.

Yet another review by Frankel and Simmons in 1976 compared

different behavioral treatments for controlling behavior in individuals with intellectual disabilities or schizophrenia, and noted that in terms of immediate effects, punishment was the quickest means of suppressing behavior.

For longer-term effects, timeout programs fared the best, followed by differential reinforcement techniques. In marked contrast to the short-term effects, punishment and extinction programs seemed to have least durable success.

In summary, the literature review generally supports short-term reduction of SIB and aggressive behavior with ESD use. No consensus was seen for long-term benefits, with many researchers reporting that behaviors return when the device is inactive or removed. Finally, though data for this is limited, the role of stimulus intensity may impact the magnitude and duration of effect.

Limitations of the systematic literature review of benefits include the lack of prospective, randomized, placebo-controlled or comparative trials, different devices and device administration, non-systematic assessment, lack of statistical analyses, and non-adherence to modern research and publication standards, with the majority of articles being published in the 1960s and '70s and consequently not adhering to modern study conduct and publication standards.

A total of 27 articles containing clinical information were

identified in the systematic literature review of potential risks associated with ESD use for aversive conditioning. This included one prospective case-control trial, one retrospective chart review of 60 patient charts, and 25 case reports or case series reporting the experiences of 66 individuals. Sixteen other case reports and case series, those identified in the literature review of benefits, did not mention assessing adverse events or the occurrence of adverse events.

As with the review of benefits, the highest-quality publication was a case-control study of eight subjects and eight matched controls by Duker and Seys in 2000. In this article, there was no systematic report of adverse events by subject.

One retrospective review of 60 subjects noted only one negative side effect, temporary discoloration of the skin that cleared up in a few minutes or days. However, the authors of this article went on to state, temporary emotional behaviors, a temporary tensing of the body, or attempts to remove the device or grab the transmitter, noted during treatment, were classified as immediate collateral behavior and were not considered adverse events.

Twenty-seven case reports and case series, reporting on 66 subjects, contained specific adverse event report information. They are listed in Table 4 of the Executive Summary.

Review of the case reports and case series identified the

following potential adverse events:

- Anxiety
- Fear and aversion or avoidance
- Substitution of other negative behaviors
- Burns or other tissue damage
- Depression or crying
- Pain or discomfort
- Neurological symptoms
- Other negative emotional reactions or behaviors

Several other articles were identified examining the use of ESDs for aversive conditioning for other indications. Twelve of the 15 articles did not report any adverse events or if adverse events were assessed. However, the other three articles identified the following potential adverse events:

- Anxiety
- Psychotic delusions
- Headaches
- Restlessness
- Mild dysphoria
- Mild transient depression

Twelve review articles examining potential risks of ESD for aversive conditioning were also identified. Seven of the 12 acknowledged the possibility of negative emotional reactions such as fear, avoidance, aversion,

anxiety, and depression. Five of the reviews also noted the possibility of retaliation, increased aggression, and substitution of one injurious behavior for another.

Two reviews concluded that ESD use for aversive conditioning is not associated with any significant adverse events. One review by Lichstein and Schreibman in '76 contended that physical discomfort and emotional reactions are required in order for the treatment to be effective. Therefore, these effects may be considered indicators of the main treatment rather than unwanted side effects.

In summary, potential adverse events identified in the systematic literature review include pain, physical injury such as burns, tissue damage, and neurological symptoms, and psychological adverse events such as anxiety, fear, aversion and avoidance, depression, and other negative emotional reactions.

The literature review of risks was limited by the general lack of systematic assessment of adverse events, the potential difficulty of some subjects, particularly those with intellectual or cognitive disabilities, to report adverse effects, and the evolving conceptions of disease and pathophysiology. Many of the articles reporting adverse events were published during a time when conceptions of disease and dysfunction differed significantly from our current understanding. This may complicate the interpretation of potential risks of ESD use as described in the literature

review.

For instance, adverse events may have been interpreted and reported from a different conceptual framework, a behavioral or a psychodynamic framework, and many may require translation or they may have been minimized or not recognized as adverse events, as in the case of considering negative emotional reactions as necessary or collateral.

In addition to the systematic literature reviews, other sources of information include the MAUDE database, reviews and reports submitted to FDA from independent sources, including recommendations and/or consensus statements regarding aversive conditioning from two professional or scientific organizations, prior public proceedings held on ESD use for aversive conditioning, information from manufacturers, three clinical reviews conducted by FDA staff with individuals who received ESD administration, a letter from the Judge Rotenberg Center Parents Association of three parental reports of their children's experience, and seven additional case reports of ESD use and other publicly available information.

The MAUDE database maintained by the Office of Surveillance and Biometrics at FDA, to which medical device manufacturers are required and others are encouraged to voluntarily report adverse events, contains one report of an adverse event for aversive conditioning devices. This report was submitted in 1995 from an unnamed source and describes an incidence of an inadvertent deployment of an ESD for aversive conditioning -- that is, a GED

device -- with resulting skin lesions, including two ring-shaped marks and three areas of rough skin.

Recommendations or consensus statements regarding aversive conditioning therapy from two scientific organizations were identified and reviewed. Both statements were published over 25 years ago with no follow-up or revision of position since that time.

In 1987, the Council on Scientific Affairs of the American Medical Association, in considering all aversion therapy, concluded, "when behavior is dangerous and has not improved with less intrusive procedures, increasingly aversive techniques, up to electric shock for the most severe, are appropriate." The council also emphasized that the literature for all indications is founded on single or group case studies.

In 1989, the National Institutes of Health held a conference to review the treatment of destructive behaviors in persons with developmental disabilities and to develop consensus recommendations, including various types of aversion therapy. They reached consensus that behavior reduction interventions appear to be effective in some individuals, particularly in suppressing destructive behaviors such as self-injurious behavior.

The consensus statement indicated that negative side effects of behavioral interventions have been reported, including the emergence of other forms of self-injury or other forms of undesirable behavior. They recommended that behavior reduction procedures should be selected for

their rapid effectiveness only if the exigencies of the clinical situation require short-term use of such restrictive interventions, and only after appropriate review and informed consent are obtained. Such interventions should be used only if they are incorporated in the context of a comprehensive and individualized behavior enhancement treatment package.

The New York State Education Department (NYSED) conducted site visits in April and May of 2006 to the Judge Rotenberg Center and issued a report evaluating all aspects of the program, particularly health and safety issues related to the use of ESDs for aversive conditioning. A brief summary of the entire report can be found in Section 5.3.3 of the Executive Summary.

The report found substantial risk of skin burns from the device and psychological side effects such as fear, aggression, and anxiety. It's notable that these adverse events are associated with the overall use of aversive interventions at JRC and not specifically related to ESD administration.

One student was interviewed and reported that she had been burned by the GED-4 device while taking a shower. Another student reported feeling depressed and fearful, with a desire to kill herself and thought about killing herself every day.

In 2001 [sic], the Massachusetts Department of Developmental Services, or DDS, proposed an amendment to prohibit the use of Level III behavioral interventions, including ESDs for aversive conditioning. This is

fully described in Section 5.3.4 of the Executive Summary.

The report of the proceedings included consideration of public oral and written testimony as well as a review of the research, opinions of subject matter experts, and positions taken by various organizations and associations.

The report focused on the body of empirical evidence showing that the effectiveness of other less intrusive forms of treatment that do not involve pain -- on the support of this position by virtually every local, statewide, or national organization supporting individuals with intellectual disability, and by providers and clinicians whose practice demonstrates that non-aversive treatment can modify difficult or dangerous behaviors effectively and for the long term, while aversive interventions, in addition to causing pain and anxiety in such individuals, do not have proven long-term efficacy.

It concluded, the "current standard of care for individuals with intellectual disability with the most severe behavioral challenges is positive behavior intervention and does not include aversive interventions or punishment." And as a result, DDS published a proposed amendment to prospectively prohibit the use of Level III behavioral interventions, including ESDs for aversive conditioning.

FDA reviewed complaints regarding ESD use for aversive conditioning made to the Massachusetts Disabled Persons Protection

Committee, or DPPC, from 1993 to 2013. Of 53 filed complaints, the following adverse events were reported:

- Burns or tissue injury
- Inappropriate device use
- Negative emotional reactions
- PTSD

From 2010 to 2013, FDA officials were contacted by, and met with, representatives from various national disability organizations. These organizations informed FDA that ESDs for aversive conditioning are banned in most states. They reported at least four case reports of psychological trauma and PTSD symptoms, and alternative treatments, positive environmental and reinforcement strategies, have been developed and are currently effective for severe and refractory self-injury.

In a letter to FDA Commissioner Margaret Hamburg regarding the use of contingent electric shock and other aversive interventions, disability advocates stated that ESDs for the use in behavior modification are inherently unsafe and that there are other demonstrated alternative treatments for the patient populations being treated with these devices.

Of note, FDA did not make initial contact with any professional organizations or groups and did not seek their attendance or participation in this Advisory Panel meeting.

In 2010, Mental Disability Rights International, or MDRI, an

international human rights group, published a report regarding ESD use at the JRC. Citing information from facility employees, family members of students, and independent sources, they noted adverse events, including significant levels of pain, tremors, burns, tissue injury, fear and other emotional and behavioral reactions, and the risk of psychological trauma, marginalization, or alienation.

As a result, they called on the United Nations Special Rapporteur on Torture or other Cruel, Inhuman or Degrading Treatment or Punishment to initiate an enquiry into JRC practices. In response, the UN Special Rapporteur wrote a letter, dated June 11th, 2012, to the United States Department of State, expressing concerns about JRC's aversive conditioning program.

A follow-up investigation was initiated by a second UN Special Rapporteur in 2012. The report called for an absolute ban on all coercive and nonconsensual measures, including electroshock procedures. In an addendum, the Special Rapporteur determined that the rights of the students at the JRC, subjected to Level III aversive interventions by means of electric shock and physical means of restraint, have been violated under the UN Convention against Torture.

In connection with FDA compliance activities regarding the use of uncleared devices -- that is, the GED-3A and the GED-4 -- JRC has provided the following information: patient case summaries of 86 individuals, 66 of

whom have had treatment plans that included GED use. They reported that all 66 had significant reduction in SIB or aggressive behavior with ESD application.

In addition, according to the records, no adverse events were reported for any of the patients' GED complaint files, which included one report of a burn that was determined not to be related to GED use.

A meeting between FDA's Office of Compliance and representatives of the JRC was held on January 9th, 2013, at which the JRC presented anecdotal information about the benefits of the device, including the specific benefits to the daughter of one of the doctors present.

In the policy document with the heading "JRC Policy," entitled "Procedures to Facilitate the Assessment of Possible Collateral Effects," the document acknowledges potential negative side effects associated with Level III aversive procedures.

It states that "JRC staff must be vigilant in assessing whether aversive interventions are causing any short-term or long-term collateral effects such as increases in aggression, escape behaviors, emotional reactions, sleep difficulties, and any other physical or emotional reaction or change. Such changes could include not only immediate physical observation, such as temporary redness of the skin, but also longer-term nonphysical consequences such as nightmares, intrusive thoughts, avoidance, mistrust, depression, and flashbacks."

FDA clinicians have interviewed three individuals that were referred to the FDA who have received ESD administration for aversive conditioning.

The first individual was placed on the GED-4 device. He reported that the stimulus felt "like a thousand bees stinging you in the same place for a few seconds." The individual did not feel that ESD was effective. It only made him fearful.

In terms of adverse events, he reported burns that lasted a few days, but no other long-term physical effects. With the device applied, he described being in constant fear and not having any idea of when one might be shocked or why. He reported ongoing psychological effects out to five years after ESD administration, including flashbacks, describing panicky moments when reminded of shocks, a general fear of being controlled, and a dislike of authority.

The second individual reported that he was on the GED-2 device. He described the stimulus as feeling like a "bad bee sting." He felt the device worked for his behaviors while he was on it, but then didn't work after they took it off.

In terms of adverse events, he said he got many burns on his skin, but no permanent marks or scars. While he was on the device, he was anxious and afraid that he was going to get shocked. He denied any long-term effects such as nightmares, flashbacks, other PTSD symptoms, or

depression. He is currently at a different residential facility that does not employ ESDs and stated that his current treatment is helping to control symptoms as much as any other past treatment has.

The third individual was treated with two types of devices, the GED-3A and GED-4, over a seven-year period. She described the shocks as being extremely painful. She said the device made her feel constantly anxious and on guard.

In terms of potential benefit, she feels that the device may have helped some individuals, but it did not help her. In her case, she did not feel in control of her self-injurious behaviors, with urges that continued to build if they were not relieved. ESD use did decrease the self-injurious targeted behaviors, but this did not address the underlying condition. She said that she found new and secret ways to injure herself. She feels that the ESD treatment did not help her, and in fact made her feel worse.

As a result of the ESD administration she reported burns, scars, loss of sensation and numbness, muscle spasms, pain, heart palpitations, seizure, anxiety, fear, depression, suicidality, nightmares, flashbacks, and reexperiencing symptoms. She stated that her trigger was hearing the sound of Velcro or seeing a wallet being opened, as these things were associated with previous ESD administration, and the result of that was causing extreme anxiety.

On one occasion, after receiving seven administrations to the

leg, she experienced paresthesias and loss of sensation and numbness to the leg. She notes that these symptoms lasted about one year.

Currently, she is at a different residential facility that does not use ESDs. She reported feeling and functioning much better with the current treatment. She said that ESDs for aversive conditioning might seem like it was helpful to someone observing from the outside, but "it's not a life that anyone would want to live."

In 2013, the Judge Rotenberg Center Parents Association sent a letter to FDA to describe the impact, from a parent's point of view, of eliminating access to the GED-3A and GED-4 from specific patients. These letters described the severe physical harm their children inflicted on themselves and the countless placements and treatments, including cocktails of dangerous medications they tried unsuccessfully to prevent such injury.

They further explained how JRC's treatment program, including the GED-3A and GED-4 use, was able to stop children from engaging in dangerous behaviors, allowing them to be free from physical and emotional harm, and for the first time in their lives, to learn and to be happy. The letter states that the premature termination of the use of the device will cause great and, in some cases, permanent harm. In addition, the letter presented seven case reports that were also supportive of GED use.

In the past several years, several media reports have been published regarding the use of the GED device at the JRC. Within these

reports there have been claims of pain, burns, and physical and psychological consequences, including depression, suicidality, and PTSD. There have also been at least three media reports which were supportive of the use of ESDs for aversive conditioning.

In terms of evaluating the quality of the information that's reviewed, it's important to note that each source of information suffers from some limitation.

While the published scientific literature represents the highest-quality information available, it suffers from the relative lack of scientific method applied in the investigations, the absence of systematically conducted, well-controlled, prospective investigations, the prominence of retrospective case report studies, and the variable quality of those reports.

In addition, it's important to consider the possibility of bias in the published literature. Bias may result from a general tendency to publish positive results over negative results. In the published literature, given that only 3 of 105 total individual reports were negative, this may be a possibility. Some authors also note the possibility of bias against reporting adverse events.

Carr and Lovaas in '81 in their review opined, "In light of the intrusive nature of shock treatment, it is puzzling that so few negative side effects have been reported. In interpreting the existing literature, we might be wise to consider the possibility that some investigators have been

predisposed to see only the positive side effects."

Israel and colleagues in 2008, as previously reported in their retrospective review of 60 patient charts, noted that emotional reactions or behaviors were considered immediate collateral behavior and therefore were not considered adverse events.

The MAUDE database offers only one adverse event and therefore has little information for our analysis.

The position statements by professional and scientific organizations, while systematically conducted, suffer from the fact that they deal with aversion therapy in general and not ESD for aversive conditioning specifically. They were conducted over 25 years ago and do not take into account more recent developments in the field.

Independent and governmental reports were conducted in response to certain situations and, as a result, their conclusions may be influenced by those circumstances.

Manufacturer and advocacy groups may view the issue from a particular perspective and may represent that perspective in their positions.

Direct clinical interviews and parental reports, while offering more direct information of device use, may suffer from issues of selection bias because only the most motivated may take the time and effort to share their experiences.

And the other sources of information, namely, media reports,

do not systematically assess benefits or risks and may have been developed within a specific agenda. As a result, the following conclusions should be considered cautiously.

In terms of benefits of ESDs for aversive conditioning for SIB and aggressive behavior, considering all sources of information, short-term reduction of SIB and/or aggressive behavior may be supported, while longer-term benefits are less well established, with a possibility of relapse with device withdrawal.

In terms of risks, a comprehensive list of potential adverse events that may be associated with ESDs for aversive conditioning from all sources includes:

- Other negative emotional reactions and behaviors
- Burns and other tissue damage
- Anxiety
- Acute stress and PTSD
- Fear and aversion or avoidance
- Pain and discomfort
- Depression and suicidality
- Substitution of other negative behaviors, including aggression
- Psychosis
- Neurological symptoms and injuries.

This concludes the section on the benefit/risk assessment of ESDs for aversive conditioning. The next speaker is Dr. Michelle Roth-Cline, who will present ethical considerations.

DR. ROTH-CLINE: Good morning. My name is Michelle Roth-Cline. I am a pediatric ethicist at the Agency, and I'm presenting today on ethical considerations in the use of aversive conditioning ESDs on behalf of myself and my colleagues, Drs. Nelson and Goldkind from the Office of Pediatric Therapeutics and the Office of Good Clinical Practice at the FDA.

The FDA literature review has found limited safety or effectiveness data on the use of aversive conditioning ESDs for the treatment of self-injurious or aggressive behavior. Additional data from adequate and well-controlled trials may be helpful to better inform this risk assessment. However, the Agency has identified serious concerns regarding the protection of the rights, safety, and welfare of any subjects in clinical investigations in which ESDs are used on human subjects, and the permissibility of such studies under FDA regulations for both children and adults.

These concerns exist irrespective of whether the device is banned because, as noted early, a ban may or may not apply to devices that are currently used on individuals. It is my task today to share these concerns with the Committee. In addition, I would like to remind the Committee that you will be asked later to opine on circumstances, if any, under which aversive conditioning devices may be studied on human subjects.

The topics I will cover today include a brief review of the additional safeguards for children, followed by an application of those principles to the use of aversive conditioning ESDs in children. I will also touch briefly on the risks and potential benefits of ESD use in the clinical setting. Finally, the Agency is aware that although the use of ESDs often began during adolescence, the use of these devices has continued in some cases into adulthood. I will therefore also comment on the risks and benefits of ESD in adults.

So under FDA's ethical and regulatory framework for children, clinical investigations must be restricted under sort of three different pathways, if you will, and the first pathway you see is the low-risk pathway. As you see, there are two low-risk categories, which are minimal risk and a minor increase over minimal risk. Greater risk is acceptable under the second category, but only if the research offers children the potential for direct medical benefit. In addition, the research must present risks that are justified by the potential benefits, and the balance of risks and benefits must be at least as favorable to the children as any available alternative treatments.

The last category is for research that is not approvable under the above two categories. As a practical matter, it's not often used because it requires that a protocol be reviewed by the Pediatric Advisory Committee, with a final determination on the acceptability of the protocol by the FDA Commissioner. So I'm not going to consider that further today.

In terms of applying the additional safeguards, the Agency has determined that the risks of ESDs, which may include depression, anxiety, and PTSD-like symptoms, as outlined in the JRC Policy document and in other case reports, exceed either minimal risk or a minor increase over minimal risk. For that reason alone, research under this lower-risk pathway would not be approvable. Therefore, research using aversive conditioning ESDs would have to be considered under the higher-risk pathway that I noted.

This pathway requires that the devices present a medical benefit to the enrolled child. In addition, the risk must be justified by the anticipated benefit, and the balance of the risks and benefits must be at least as favorable to children as any available alternatives.

So in the next two slides, I'm actually going to discuss alternatives before the justification of risk, so the opposite order in which it's listed on the slide.

So let's consider the application of this criterion on alternatives to aversive conditioning ESDs. Remember, the risks and benefits of ESD use have to be at least as favorable to children as any available alternative approaches for treating self-injurious behavior. As a general principle, the least restrictive or burdensome intervention that controls the self-injurious behavior ought to be used. There's no disagreement that ESDs are a highly restrictive intervention that ought be used only when other treatment options have failed. That's what's stated in the labeling.

So it follows that the only population in whom ESD use ought to be considered are those persons who are truly refractory to, or unable to tolerate, adequate treatment attempts of all other less restrictive interventions as administered by people with the appropriate training and expertise.

Now, even if we identified the highly refractory population I outlined in the last slide, the potential benefits of a reduction in self-injurious behaviors in that population would still have to outweigh the risks of the device. So the question is what information we have on the risks and benefits.

You've just heard that case reports and case series suggest that there may be a short-term reduction in self-injurious behaviors with device use. However, this literature review also raised concerns about potential serious risks, and there had been no systematically collected data on long-term risks or benefits of the use of the device.

So the Agency is concerned that the harms associated with the use of aversive conditioning ESDs may not justify the potential benefits, even in populations that may be considered refractory. And thus the use of these devices in clinical investigations may not be approvable under 21 C.F.R. 50.52.

We also note that the language under this category about risks and potential benefits, in light of the alternatives, was explicitly based on considerations a clinician might use when determining whether a particular

treatment was appropriate for their individual patient. For this reason, the Agency is also concerned that the clinical use of these devices may not be justified even in patients that may be considered highly refractory.

Finally, a few words about ESD use in adults. Our regulations require that the risks of the study are minimized, that the risks are reasonable in relation to anticipated benefits and knowledge that may result from the study, and that selection of the subjects for the study must be equitable.

The Agency is concerned that risks to subjects are not minimized and that the rights, safety, and welfare, particularly of subjects with developmental disabilities, would not be adequately protected if a less restrictive therapy exists with a more favorable risk/benefit profile.

So to summarize. The Agency is concerned that the research use of aversive conditioning ESDs is not approvable under the additional protections for children at 21 C.F.R. 50, Subpart D.

We are also concerned that the potential benefits of aversive conditioning ESD use may not outweigh the risks in a clinical setting.

Finally, we are concerned that the risks to adult subjects may not be appropriately minimized, and that the rights, safety, and welfare of subjects with developmental disabilities may not be adequately protected.

For final comments from the FDA, I will turn the podium back over to Dr. Bowsher.

Thank you.

DR. BOWSHER: Hi. My name again is Kristen Bowsher, and I'll provide a brief summary of FDA's presentation today.

To repeat why we are here today, FDA is convening this Advisory Panel meeting to seek scientific and clinical expert opinion on the risks and benefits of ESDs for aversive conditioning and to obtain recommendations that will assist the Agency in considering whether or not to ban these devices.

FDA has presented a lot of information today for consideration, and additional information will also be presented to you throughout the day.

When determining whether there is a substantial and unreasonable risk of illness or injury, the Panel should weigh each of the following, taking into consideration the lack of high-quality data:

- the potential risks and benefits of ESD use;
- the potential risks and benefits of alternative treatments; and
- the potential risks of leaving patients untreated or inadequately treated (which may include a greater risk of morbidity or mortality) by the use of potentially ineffective therapy.

Again, FDA will be asking the Panel to provide feedback on the following:

- risks and benefits associated with other treatment

options for this population;

- risks and benefits of ESDs for aversive conditioning to modify undesirable behavioral characteristics in patients who exhibit SIB and aggressive behavior;
- whether ESDs for aversive conditioning present a substantial and unreasonable risk of illness or injury
- potential approaches to risk mitigation;
- the risks and benefits of applying the ban to devices currently in use by patients; and
- whether a clinical trial could be conducted to evaluate ESDs for aversive conditioning for the treatment of SIB and aggressive behavior.

This concludes FDA's presentation today.

DR. YANG: Great. I would like to thank the FDA speakers for all of their presentations.

We will now proceed to the brief clarifying questions for the FDA from the Panel. For efficiency, please raise your hand to indicate to Ms. Russell and me that you have a comment or a question and you will be called to speak in order. When you are invited to speak, please restate your name for the transcriptionist, then ask the questions or comment. Note that there will be time this afternoon for questioning the FDA during the Panel deliberation session.

Does anyone on the Panel have a brief clarifying question for the FDA?

Oh, Dr. Peña.

DR. PEÑA: Yes. I'd just like to note to the Panel, for the record, as a general issues matter for an entire class of devices, FDA's presentation was not intending to identify any particular manufacturer or manufacturers, but more so really all the information the Agency has taken into consideration in an effort to arrive at this public Advisory Committee meeting. We're seeking the scientific, clinical, and professional opinions of this very Panel today.

DR. YANG: Thank you, Dr. Peña, for that clarification.

Okay. So why don't we start on the end, then, with Dr. Kim and then Dr. Stebbins.

DR. KIM: I have two quick questions, one for Dr. Bowsher and one for the ethics analysis team.

The first question is that your slide said that the GED-4 is in violation, so I just would like you to clarify. Given the material you sent us, that seems to show that the FDA actually changed their mind and it's in the process of determining whether there are violation signs. I know this is a technical point, but I just want to get a sense of whether this center willfully violated, knowing for the 10 years that they were in violation, and if that's your understanding. That's the first question. That would be a yes or no

answer, I guess.

The second is for the ethics team. You said the Agency is concerned. So I was just curious. It was an analysis with kind of -- are these conclusions of the analyses or just concerns that you want us to consider? Because, unlike the previous presenters, you presented what seems like conclusions to an analysis.

Thank you.

DR. BOWSHER: For the first question, I'll turn it to Mr. Amatrudo to answer.

MR. AMATRUDO: Again, I'm Vince Amatrudo. I'm an attorney in the Office of the Chief Counsel at FDA.

If I'm understanding your question correctly, you're asking about the status of the GED-4 or the GED devices currently in use by JRC, whether FDA changed its mind. I believe that JRC will present today. That is accurate. We originally told them in 2000 that they were exempt. However, that was incorrect, and we more recently in 2011 sent them an entitled letter and in 2012 sent them a warning letter indicating that those devices are currently in violation of the FDCA.

However, I would submit to you that these issues are not directly relevant to the questions before you today about whether the devices present an unreasonable and substantial risk of illness or injury.

Does that answer your question?

DR. KIM: Yes.

MR. AMATRUDO: Okay.

DR. ROTH-CLINE: I'm Michelle Roth-Cline.

As I understood your question, it was whether my analysis or our analysis presents, sort of, conclusions versus considerations, and I think that the answer to your question in some sense is both. You know, as I presented, the Agency has determined that research in children under some of the lower-risk pathways really wouldn't be approvable under our regulations. In other cases we have serious concerns about the risks and potential benefits, but I think that all of these things are things that we would ask you to address and think about in your comments today.

DR. YANG: Thank you.

Dr. Stebbins.

DR. STEBBINS: Yes. Glenn Stebbins.

I'm wondering if there was any information on the long-term or the lasting effect of the adverse events that have been reported.

DR. BOWSHER: Dr. Park.

DR. PARK: This is Larry Park.

So there is no systematic assessment of that. Now, we do have case reports. One of the clinical interviews said that out to five years past exposure to the device, that person was still experiencing side effects. And the -- I'm not sure. I think that's probably the longest -- at least the longest

discrete time period that was reported. Other than that, most of the reports actually didn't specify a time frame.

DR. YANG: Okay, Dr. Fost.

DR. FOST: A question for Dr. Roth-Cline. I'm confused about this requirement that all alternatives must be used before a child could be entered into a clinical trial with one of these devices. That's not generally true with new drugs. When we have a new asthma drug or a new anti-depression drug or whatever, we don't require that all children in the study must have been tried in standard known effective therapies. So I'm wondering why that principle is being applied here -- or that requirement.

DR. ROTH-CLINE: It's stated in the labeling for aversive conditioning ESDs that they ought to be used after all other treatments have been tried. You know, in addition, it's very clear that ESDs are a very restrictive intervention, and I think, as a general principle in medicine, we try the least restrictive or burdensome intervention first.

And so the idea is that, for a restrictive intervention to be justified, that is, we would want to know that these least or these less restrictive interventions have been tried and failed.

DR. FOST: So is that a regulatory requirement for just aversive conditioning, or is it in the device regs for all devices? Because, I mean, many other drugs that we test can kill you. We test cancer chemotherapy drugs. They are much more dangerous than these aversive devices.

So as a general principle, I'm confused as to why we would require that devices be held to some -- even aversive devices -- there are, admittedly, serious adverse effects, but they're not nearly as serious as the adverse effects of many drugs that we study. There's been no reported deaths from these things. Deaths are common with other kinds of drugs. So I'm unclear why the standard or the restriction would be higher for an aversive device than, arguably, more dangerous kinds of drugs or devices.

DR. ROTH-CLINE: As I stated, we are trying to think about the devices in a way that's consistent with the current labeling, and the current labeling is that the devices ought to be restricted to use in refractory populations.

In addition, as a matter of risks and potential benefits, I think that we would want to restrict the use of these highly restrictive devices to patients that really need them and really have failed other kinds of therapies.

DR. YANG: Dr. Connor, you're next.

DR. CONNOR: So I had one, and then Mr. Mikita has one, too, I think.

So my question. I think this is a technical point again, but I'm still confused by the fact that it sounds like we're being asked about specific devices that are FDA approved that no one uses. So I'm confused by our role. And granted, someone theoretically could, but it sounds like currently no one uses the devices that are FDA approved. So I don't quite understand our role

here.

DR. BOWSHER: I think you're right, in that right now we're only aware of one institution using the device, but we don't know that that's so in the future. So we're looking for your feedback on the whole class of devices.

DR. CONNOR: And if a new manufacturer came along, would they be -- so I mean, it's hard to rule on something in theory. So if a new manufacturer came along and was developing a particular device, would that likely have an easy path under 510(k)? Would it be a PMA where they would be expected to bring high-quality efficacy and safety data? Because it seems like all of these things are relevant because we're ruling on what's happening in the future, so I would like to understand what regulatory hurdle would be expected of any new device maker who would make such a device.

DR. BOWSHER: I'll let Mr. Amatrudo answer that.

MR. AMATRUDO: Hi again. I'm Vincent Amatrudo in the Office of the Chief Counsel.

To start, it's not purely theoretical. There are two models of devices currently in use that would be covered by that. If we were to ban, it would also cover new devices. So a manufacturer would be essentially prohibited from making and distributing devices that fall within the scope of whatever -- if we were to decide to ban, whatever we decide to ban.

DR. CONNOR: And the devices that you mentioned that are being used, are they devices just at the JRC, I assume, sort of the lower-

voltage or lower-current devices at the JRC?

MR. AMATRUDO: I can let Dr. Bowsher speak to the technological characteristics of the devices, but my understanding is that we cleared a particular version of the GED device back in 1994, and there are currently two different models in use at JRC. I believe one of them has similar output characteristics and the other one is much stronger. But I'll let -- if you have additional questions about their technological characteristics.

DR. CONNOR: Okay. No, that's good. I think I understand that part, then. Okay. So I appreciate that. And then I think Mr. Mikita has --

MR. MIKITA: Okay. I don't turn my head well to the right, so don't be offended if I can't see you eye to eye.

I have a couple of questions, first of all, that I'd like to clarify for the record. Dr. Park, during your remarks about the Massachusetts Developmental Disabilities report, although the report occurred in 2011, you stated that it was 2001. I want the record to reflect that it was 2011.

I'd like to go back and give an overall opinion/concern. I'd like to understand from the FDA's point of view -- and I don't know why a chronology wasn't given. I think it would have benefited us. And it goes back to what Dr. Connor said. I'd like to understand why all of these devices were phased out all across the United States, when they were phased, why they aren't being used in any other state in this country except this one location in one state, in one center. Why is that? No one has bothered to provide this

Panel that question. It would have been great to see, from the 1960s, '70s, the prevalence of usage of these devices. Then in the '80s and '90s, apparently state after state banned them and now we're just down to one particular site. Why is that? So let's have an answer to that question.

Then I want someone to answer the question about the clinical reviews. Why were they done? Why did FDA just do three clinical reviews and why did FDA do them over the impersonal medium of a telephone call and not individually meet with the patients at their perspective? Why wasn't it done on site so it's kind of sanitary, sterile way?

Thank you very much.

DR. PARK: Hello, this is Larry Park again.

Yes, thank you for that clarification. I believe I did misspeak when describing the Department of Developmental Services report. And that did come out in 2011. So thank you for that clarification.

The second point. I'm not sure I'm the best person to speak to that, but I'll give it a stab. As you noted, there were a number of devices that we talked about that had been cleared for marketing in the United States, and as we just recently discussed, to our knowledge, we believe that there's only one center using an ESD device. Not a cleared one, but one that related to a cleared one.

As to why that is, you know, I'll give my opinion. I can only offer my opinion on why that is. But part of it is that some of these

companies may have been in business earlier on, and as the treatment became less popular, then those companies presumably went out of business. So, again, to our knowledge, we only know of one manufacturer that's making that device. I think that some of it is economics.

I also stated in my presentation that a number of states have banned the device use. So I think that there's some sentiment throughout the country that this shouldn't be a device that's being used. And that may also feed into the fact of why there's only one place in the United States, only one manufacturer that's currently active.

With regard to the third question, in terms of the clinical interviews -- so as I stated with the professional organizations and advocacy groups, that we did not go out and solicit any opinions or input, that is also the case with the clinical interviews. The clinical interviews were people that were referred to us from outside sources. And if that happened, then we would follow up on that. And I do apologize that all the interviews were conducted over the phone, but that was done for practical reasons.

DR. YANG: Thank you.

So next, Dr. Armstrong.

DR. ARMSTRONG: Thank you.

I just have three questions, and one is related to a term that was used in the presentation, that in the midst of some variability, I guess is the best way to say it -- in terms of methodology -- and that was the word

"refractory." Was there a consistency in the definition of what refractory meant in the studies that were being reviewed? I'll stop with that question and then follow up.

DR. PEÑA: And can I just -- before Peter comments, just to go back to the last question about the phase-out. You know, the marketplace often determines the share of devices that are beyond FDA's mission of looking at the safety and efficacy of whether a device is ready for market. So as alternative therapies become available, certain technologies may fall into disuse. I'll also ask the team if they have additional considerations after this session. If there's information that we can share, we'll also circle back on that.

DR. COMO: Yes, thank you. I'm Peter Como. Again, yes, thank you for that question. It is a challenging question.

To my knowledge -- and Dr. Park may also address this -- in our review of the literature, we really were not able to identify any studies in which the prime purpose of the study was to identify a refractory patient population.

However, in our review of all of the different types of treatments, including ESDs, it was clear to us -- or at least to me -- that when we look at our cleared indication for these devices, we did -- and this was done back 20 years ago, where it was indicated for people who have failed other or all forms of treatment. So it got us to thinking about, well, what are

the challenges and what are the issues in identifying treatment failure, because it was never really specified in the cleared indication.

So my slide was really trying to point out that (a) we don't know if there truly is any data out there about a refractory population and what that population might look like, but then, to sort of counterbalance that, our thoughts about what treatment failure might represent, because we had put it in our labeling many years ago.

Does that answer your question?

DR. ARMSTRONG: Yes, it does. Thank you. I think one of the observations of both your presentation and some of the other materials that were presented to us was that -- particularly in presentation by individuals, which was part of the data that you used -- it was not clear in those statements what refractory actually meant. And I think it's a critical consideration for us. Thank you for that answer.

The second question that I had is, if we were looking at this as an oncologic drug or something else, one of the things that we would very likely be seeing is some report in an area where systematic human studies have been limited, that there may have been some preclinical studies that would have looked at some of the safety issues of continued use. Are there preclinical studies that we should be considering?

DR. COMO: To my knowledge and our review of the literature, we did not uncover any -- well, I should step back. That's not entirely true.

And I think in the Executive Summary, we do cite that there are a number of animal studies that have really looked at -- this was more in line with trying to understand the putative biologic etiologies of self-injurious behavior or aggression.

So there are a number of hypotheses that have been purported, a lot of them based on animal studies using some manipulation of the dopaminergic or serotonergic pathway or some other physiologic or biochemical manipulation in various animal studies. But to my understanding of the literature, it was really aimed at trying to get a sense of what might be the underlying path of physiology, because if we could identify that, it might suggest a particular form of treatment. For example, if indeed these behaviors are due to some dysfunction of the serotonergic pathway, then we do have a class of drugs that seem to affect those pathways and therefore might have a beneficial effect in treating human behavior.

DR. ARMSTRONG: I guess that's helpful, but those studies seem to really look at mechanisms rather than there's been no clear designed study with an animal model to examine the safety and efficacy of long-term exposure.

DR. COMO: To my knowledge, that is correct.

DR. ARMSTRONG: The final question I had -- and this is a very difficult one with this particular population because we are dealing with individuals who have an intellectual or developmental disability, and often it's

tossed to the side. But the NIH has held some recent conferences examining relationships between pain and neuropsychological and neurocognitive function. Has there been any evidence of examinations of decrements of cognitive functioning in this population as a result of this exposure? I didn't see it on the AE list.

DR. COMO: Again, in our review of the literature -- actually maybe, Dr. Park, since you reviewed that -- but to my knowledge, we did not uncover that. I think part of that may be limited by the fact that in some of these studies, the intellectual and cognitive capacity of the individual was sufficiently compromised, that the ability to detect further decline or changes via neuropsychological or other types of testing might have been impossible because the individuals had already basaled out at a lower level. But I'm not aware of any studies that have specifically spoken to cognitive or neuropsychologic adverse events as a result of using these ESD type of treatments, or any other aversive treatments for that matter. I did mention the fact that there are other aversive treatments that are out there.

DR. PARK: This is Larry Park again.

I would just confirm what Dr. Como said and also add that in the articles that were uncovered by the search, there were actually no articles that even reported that they looked at cognitive adverse events. There were no reports of cognitive adverse events.

DR. YANG: Okay, for the rest of this session, let's do Dr. Dorsey

and then Dr. Miles, followed by Dr. Kim.

Dr. Green, you'll be first this afternoon in the Panel deliberation session.

Dr. Dorsey.

DR. DORSEY: Hello. Ray Dorsey. I have just a question for clarification for the FDA.

Is the indication for electrical stimulation devices for the treatment of self-injurious behavior and aggressive behavior implying that both need to be present?

DR. BOWSHER: So the indications were mainly for self-injurious behavior, but we also included aggressive behavior because that was highly reported in the literature.

DR. DORSEY: Does that mean that both need to be present for the --

DR. BOWSHER: Oh, no, that was kind of an "and/or."

DR. DORSEY: So if an individual just has aggressive behavior, is the device indicated?

DR. BOWSHER: Our devices are not indicated for just that, but we are considering that in today's deliberations.

DR. DORSEY: Thank you.

DR. YANG: Dr. Miles.

DR. MILES: I have a question for FDA. When you notified the

Rotenberg Center that the device they were using did not fall within the original exemption, did they respond back to you with any information as to why they modified the device and give any rationale or data to support that modification? And I have a second question as well.

MR. AMATRUDO: I'm not sure of the extent to which this is relevant to the issues before the Panel today. I can just say briefly that, back in 2000, we mistakenly informed them that they were covered under an exemption in our regulations relating to use by practitioners in the practice of medicine. In 2010, 2011, we determined that is not the case. I believe they assert that in their presentation, that that is true. We disagree, they are not exempt. We consider both the GED-3A and the 4 to be in violation of our statute for not having clearance or approval as required by our statutes.

JRC has made arguments and presented information about these devices. I think that's probably a better question to ask JRC during their presentation. There might be confidentiality issues there, so I'll let JRC address what they've submitted to FDA.

DR. MILES: Well, I think it is relevant because, if additional scientific information came to FDA with regard to these specific devices, that's within the purview of the Committee.

But that being said, the second issue pertains to dosing. It seems to me that critical to any medical device is the capacity to dose the material, in this case an electrical shock. They talk about dosing in the sense

of keeping it away from the heart. But the dose would also be affected by things like sweat, fat, the fat over the muscle area where it was applied, perhaps the location of the electrode relative to major nerves, for example, the tibial nerve. And the question would be, is there any dosing instruction that goes with this, other than keep it away from the heart?

DR. BOWSHER: So the current devices that we've seen and cleared at the FDA are single-output devices with no ability to adjust the output.

DR. MILES: The question pertains to dosing in terms of the application of the device to the individual, checking for skin fat, that kind of thing, or wiping off sweat.

DR. BOWSHER: Currently, in the instructions for use, there's nothing regarding that. But the company that currently uses it may be able to discuss that and their practices.

DR. YANG: The last -- no.

MR. AMATRUDO: A follow-up to the previous question. The issues regarding the violative status of their current devices relate to the changes that they made from the cleared device. The questions that we're focusing on today are about whether the risks posed by the device are substantial and unreasonable with respect to both the cleared device, other cleared devices, the uncleared devices -- so the whole group. And it's focused on the risks and whether they are substantial and unreasonable and not --

there are no questions relating to their comparison to the predicates, which is the issue with a 510(k).

DR. YANG: Okay. And if there are no other questions, then, Dr. Green, my apologies, but we'll start with you this afternoon in Panel deliberations. Let's give fair timing to our other presenters. So let's go ahead and take a 10-minute break.

Panel members, please remember not to discuss any meeting topics during the break amongst yourselves or with the audience. We will resume promptly at 10:25 a.m.

(Off the record.)

(On the record.)

DR. YANG: All right, we're going to start with the next session. So we will now hear from one of the five industry manufacturers of the GED aversive conditioning devices.

For the record, the four remaining manufacturers that are not present during -- sorry -- are not presenting today were sent letters granting them an opportunity to present during this time. However, no responses were received to the FDA on their behalf indicating their interest. The information discussed during this section of the meeting should not be considered a representation of all of the industry manufacturers.

The following manufacturer that will address the Panel at this time is the Judge Rotenberg Educational Center.

Ms. Crookes, if you could approach the podium, please, and you may begin. Is Glenda Crookes or any other representative from JRC present?

DR. YANG: Okay, I think we can wait for that.

(Pause.)

LCDR RUSSELL: During this time, if we could ask all of JRC's presenters to please move to the first row so that you can prepare for your presentation.

DR. YANG: Thank you, Ms. Crookes. Please begin when you're ready.

MS. CROOKES: Good morning. My name is Glenda Crookes, and I am the Executive Director of the Judge Rotenberg Educational Center.

JRC is a special education school and treatment facility founded in 1971 for both children and adults with severe behavior disorders. We are located in Canton, Massachusetts, and have 241 students enrolled in the program. We do use an aversive conditioning device in the program and have since 1989, for 25 years, very safely and effectively. Currently, 60 of the 241 students have an aversive conditioning device as one component of their behavior plan. There are no current students under the age of 18 utilizing the device.

There are many agencies responsible for the oversight of JRC. We are licensed by the Massachusetts Department of Elementary and

Secondary Education as a special education school. We are an approved out-of-state provider for both New York State and Illinois. Our adults day program is licensed by the Massachusetts Department of Developmental Services, which also provides a special certification to JRC to use the aversives. Our group homes are licensed by both the Massachusetts Department of Developmental Services as well as the Massachusetts Department of Early Education and Care.

We currently serve students from 11 different states all over the country. Some of those states have banned the aversive therapy within their own state but send them to JRC for the treatment through a waiver process. All of these states that send the students to the program must ultimately approve the treatment via the student's individualized education plan or the individualized service plan.

We do everything we can at JRC to keep the environment comfortable, happy, and upbeat, while designing very individualized education and treatment plans around the specific, very unique needs of the students.

All of the students at JRC receive state-of-the-art behavioral programming. All incoming students receive thorough evaluations, including assessment of behavior function. We use a variety of therapies and educational tools, including constant reinforcement of positive behaviors as well as the teaching of positive behaviors to replace those behaviors that are

harmful. Additional treatments such as medications and psychotherapy and counseling are utilized if indicated.

The students that JRC treats with the aversive conditioning are those with extraordinary behavior disorders. They typically have been treated ineffectively with a wide range of therapeutic interventions over extremely long periods of time. They come to JRC typically after having been expelled or rejected from 12 to 15 prior placements. No other treatment facility is willing to take these kids in most cases. They have not improved with comprehensive behavioral programming alone.

This young lady came to JRC heavily medicated, restrained to a bed, via ambulance. That is the typical arrival of many of our students. Just a short two years later, she had gained the necessary behaviors and skills for competitive employment in the community.

The data demonstrate a clear clinical need for these devices. Those utilizing this therapy at JRC have failed at all other treatment centers. They have failed at JRC prior to the utilization of the GED devices.

Our parents are often told that there are other options. They are not for these individuals. They've all been tried and have all failed.

The data demonstrates the effectiveness in reducing harmful behaviors. They are no longer a threat to themselves or others. They are happy, they are healthy, they are medication and restraint free, and for the first time in their lives they are learning. We have seen students that couldn't

even feed themselves, dress themselves, they were not toilet trained, and to see the changes in their existence after the implementation of the treatment is miraculous.

The data clearly demonstrates that the aversive is safe and does not present a substantial risk of injury, and the risk/benefit ratio supports the continued availability of these devices.

The GED is an aversive conditioning device that was developed by JRC. It provides a harmless two-second electrical stimulation, contingent on extreme aggressive or self-injurious behavior, to reduce or eliminate the behavior. It is produced at JRC and only used for clients at JRC. It is not distributed or marketed for sale and never has been.

The device itself has a battery attached to it, with an electrode typically applied to the arm or leg, and a remote transmitter.

There's an extensive regulatory history here and some of the questions earlier remarked on that. The GED device was cleared in 1994 through a 510(k) clearance. In 2000, FDA showed up at JRC for an unannounced inspection and determined at that time, while the 3A device and the 4 device were in service and in use at the time, that it was no longer -- the 510(k) process no longer was required, that this device was under the exemption, the medical device exemption.

In 2011, however, FDA abruptly changed their position. They came to JRC again, 11 years later, issued an untitled letter and in 2012 a

warning letter stating that a new 510(k) notice for the GED devices was now required. We have been working with them since that time on submitting a new 510(k). However, upon their request, we submitted a pre-submission to the 510(k). A bit over a year ago we submitted the pre-submission. We scheduled a meeting with them to discuss the pre-submission and had not heard from them until two weeks ago regarding this meeting.

The GED device itself is remotely activated to deliver an electrical stimulation to the patient. It is administered by trained staff who directly observe the behavior, the behavior that has been identified by the clinician and approved by the court. It's a two-second pulse that delivers a DC current.

The stimulus generated for creating the stimulation for the 3A delivers a 15 mA stimulation, whereas the GED-4, used for patients with more difficult behaviors, delivers a 41 mA stimulation. It's typically placed on the arm or leg and, as indicated on the label, never placed on the spine, chest, genitals, head, top of the hand or foot, or the lower quadrant of the buttocks.

There is a subgroup of patients who exhibit serious self-injurious, harmful, and aggressive behaviors. They're a danger to themselves and others. All medications -- I can't say all -- medications and all other therapies at other institutions and JRC have failed to safely and effectively treat these behaviors.

They come to us restrained. They're in helmets, they're

bloodied, they've harmed themselves to the point where parents don't know what to do, and we know we have a potential solution. The positive behavior support techniques at JRC hadn't worked, at all other institutions have not worked.

And there are several requirements before we can even move forward with the GED. The other therapies have to be proven to have failed. The parent/guardian must provide written informed consent, which can be withdrawn at any time. A Ph.D.-level licensed psychologist or board certified behavior analyst must prepare a treatment plan. A peer review committee must review the plan and deem it appropriate. The school district or the agency that referred the patient to JRC must approve the treatment plan and incorporate it into the IEP or ISP. A physician must certify the absence of any medical contraindications. A human rights committee, independent from JRC, must approve the treatment plan.

And, finally, the treatment plan must be authorized by a Massachusetts probate court. The judge will assign an attorney to represent the client, separate and apart from JRC or the parent. That attorney will hire his or her own experts to evaluate the treatment. And the court must ultimately approve the treatment, review it each year, and reapprove it.

The stimulus is always delivered contingent upon harmful behavior. The staff must directly observe the behavior. And we have a verification procedure, that two staff must verify that that behavior is in fact

indicated for the use of the device. Each patient is evaluated by a nurse after receiving a stimulation. A staff member must visibly check the site. And the electrodes, regardless of whether the device was activated or not, must be rotated every hour or after every application. Weekly evaluations are required by the attending clinician. However, they tend to see them much more frequently, almost daily.

Each activation is documented on a behavior tracking sheet. It's documented in a database, and it's documented via 24-hour video monitoring to ensure proper implementation and to allow for the clinician to go back and review the incident.

Any misapplication or spontaneous application of the device is rare, and we report it. Any JRC personnel that had a confirmed misapplication is immediately terminated.

I'd like to take this opportunity to invite any FDA clinicians to come and visit the program to see how everything works in its true environment.

And I'd like to introduce Dr. Nathan Blenkush, who will talk about the clinical data.

DR. BLENKUSH: Thank you. Good morning, everyone. My name is Nathan Blenkush. I am the Director of Research at the Judge Rotenberg Center, and I'm a board certified behavior analyst.

I want to start off by just pointing out that a severe behavior

disorder is an absolutely devastating condition, and if you spend moments with people who emit these types of behaviors and you examine their treatment history and you talk with the people who know and love them the most, it's clear that we have to look for procedures to try to help them with these problems. And here are the options, the treatment options, that are available to these people. And I submit to you that aversive conditioning devices, as part of a comprehensive behavioral program, are very often the least restrictive and most effective intervention to address these types of problems.

Currently, we have 241 patients at JRC. Eighty-three of them have used the GED in the past at some point. Currently, we have 71 court-approved treatment plans, and of those 71, 60 are currently receiving treatment with the GED.

Before we ever start treatment with the GED, the first thing we do is try to understand the behavior through assessments, through observation, through tracking every single behavior that the person emits over the course of days and months. We have DVR footage, we have checklists and all kinds of systematic ways to investigate behavior function, in addition to all the data that comes with each person that we treat.

Currently, after that process, then we may seek court approval to use the GED and to supplement that program with an aversive conditioning device.

Once the treatment is put in place, right now, currently for our 60 patients who are receiving the GED, they're receiving less than two applications per week. That's less than two seconds of exposure to the skin shock per week. And six of the patients haven't received any applications at all in the last six months. So, again, this is showing that the treatment is extremely effective in maintaining low levels of problem behaviors.

This is a safe device. It has no long-term side effects that we've noted, no mental health side effects such as PTSD. In fact, consistent with the literature, mostly positive side effects are noted. And I'll get to more of those later. We see dramatic improvements in their quality of life.

Remember, when people come into our program, generally they are prescribed several different psychotropic medications, many of which leave them sedated and many of them leave them somnolent. They're restrained for large portions of the day. They're wearing protective equipment, arm splints, helmets. You know, I can think of all kinds of different devices that people come to our program to stop them from engaging in their behaviors. Some of them come to our program with criminal charges against them. So there is a wide range of positive effects that we see once the treatment is added.

There are some side effects. In rare cases there is mild erythema of the skin that disappears within a few minutes or a few days. And in less than 1% of the applications, we see a < 1 mm lesion that resolves in

one to two days with no scarring. We do see in some cases -- not all cases -- brief temporary anxiety just prior to the delivery of the application, and we do see avoidance responses.

But I want to point out that most of these people are requiring emergency physical restraint daily. Many of them are requiring PR injections of antipsychotic medications and other drugs. Many of them are put in timeout rooms as treatments. And all of those procedures also have avoidance responses and anxiety associated with them as well. And this procedure is only used a few times a week. So, again, it's very similar to what you would see with the other procedures.

The GED device does not cause burns. The DC current at this output cannot cause burns. The Canton police have come to JRC and looked at the clients when there's been anonymous reporting, and they have found no evidence of burns, and they've determined it false reports. We've had the Massachusetts Disabled Persons Protection Commission come in to review these reports of burns.

So our data are very consistent with what you'll see in the literature over the last 25 years. And, again, I want to point out that many of the earlier devices were not designed for human use. Our device is. And some of the devices that were used in the last 25 years have been designed for human use. And in the last 25 years there has been noted a slight local tremor during activation, no tissue damage, and again brief anxiety that

normally is limited to the early portion of the treatment, which is when the person is most likely to come into contact with the aversive conditioning device.

This procedure is effective. All of the clients that have this, they experience a meaningful decrease in their aggressive self-injuries or other harmful behaviors.

And we see a lot of positive side effects. In many people we see a dramatic improvement in the affect and the way that they present. Many of them are able to receive medical treatment that they wouldn't otherwise have been able to receive. They're able to enjoy time with their family.

Again, for a lot of our clients, they've been in psychiatric hospitals for years. They've been in a wide range of residential programs for years, throughout their entire childhood and adolescent development. This is where they grew up, in these types of programs. And they can't go into the community because they are a danger to themselves and they are danger to other members of the community. This procedure allows them to do that, and it allows them to integrate into the community, which is an ADA requirement.

In almost all cases we're able to eliminate the use of psychotropic medication and all of the negative side effects that are associated with it. And in many cases we're able to eliminate the need for

restraint and protective equipment.

So, again, 12 of the 83 that had plans no longer have court-approved plans and no longer wear the devices. Eleven additional patients have stopped using devices altogether, and six have not received any applications in the past six months. And others are in various stages of fading, where we are systematically removing the use of the GED throughout the day, starting with a few hours and increasing that duration as they do well.

This is a study that was referenced earlier. It's a retrospective study of 60 participants, and it covers a three-year period, and it pertains to aggressive behaviors. And it shows that, in all of the cases, these are people that had been in -- had a wide variety of treatments in a number of different settings, that the introduction of the GED produced at least a 90% reduction in the problem behaviors from baseline. And, again, the side effects are the same ones that we mentioned before.

This is a case study that describes seven patients who attended very well-respected and very well-regarded residential programs with very adept clinicians, a very well-intentioned and very competent treatment. And despite that treatment, after years of treatment, they were asked to leave. They were told that the procedures weren't effective and that they had to go seek other treatment. And it shows that once the GED was added, there was a significant reduction in their problem behaviors. All of the medication that

they were taking previously was discontinued, and restraint was eliminated or significantly reduced. And they all were able to make educational and vocational progress.

So there's the main effect, which is the effect on the behavior. When you arrange the GED as a consequence, there's a main effect, then, which is reducing the aggressive or the self-injurious or other harmful behavior.

But contrary to what you might think, the literature actually supports that there's a lot of positive side effects rather than negative. And these are from studies over the last 25 years, suggesting reduction in other problem behaviors that aren't treated with the GED or skin shock device. Increases in smiles, laughing, communication, more responsive to positive reinforcement -- and this is consistent with what we see at JRC.

You can imagine that many of these people spend the majority of their lives restrained. They can't benefit from -- it's hard for them to benefit from skill acquisition procedures. It's hard for them to experience many of the things that we all take for granted as far as being able to go with your family out to eat, being able to do all of the things that we can see.

And here's one example. And I could put 60 of these up here, okay, because the treatment histories are very similar. This is a young man who had early autism intervention. He went to a day program, a very well-regarded day program. He was given a wide range of medication trials. And

he came to us first as a day student and then as a residential student.

And just to give you an idea, from 2007 to 2011, this young man was restrained nearly 2,000 times for a total of 748 hours. Okay. He caused severe injuries to himself and others, concussions, broken bones. And what I always point out about him is that you couldn't even approach this young man, and if you did approach him, you would approach him like this because you were fearful of him head-butting you or biting you.

And now you can see this is a logarithmic chart here, a semi-logarithmic chart showing the frequency of his behaviors. His aggressive behaviors went from hundreds and sometimes thousand per month down to zero over the course of a few days. This is just a remarkable decrease in the frequency of his aggressive behaviors. This is his health dangerous behaviors, self-injury. It went from hundreds per month -- and, again, this is while he's mechanically restrained for large portions of the day -- to ten per month and now maintaining at around one per month. So these are just remarkable results.

This is what Andrew is able to do now. He hadn't been to a restaurant in five years. He hadn't been able to go to a restaurant in five years, and now he goes to these things on a regular basis.

This is Samantha. Samantha came to our program, and she had detached both of her retinas because she struck herself in the face 2,000 times a day if she wasn't restrained. She was expelled from a very well-

respected program. She was given a wide range of medication trials. Again, the same story, the same treatments that were used and weren't effective. She was able to have corrective surgery. She can see again. She can participate in an educational program. She can go on home visits and do things that she would not otherwise be able to do.

So there is a clear clinical need for these types of treatments. There are people all over the United States that don't get access to this, and they're restrained and they're placed on drugs, and they have all kinds of other problems, and there's a clear need for this. And, again, we seem to recognize this in the literature. We know that there is no clear understanding of self-injury in all cases, and that's why people are moving to use procedures like ECT to address these problems.

For these patients, all of the treatments had previously failed them. So if a device like this is banned, then for many of them, they're going to go back to the state of being restrained, of losing access to education, and they're going to lose access to the vocational progress they've made, and they're going to return to a life of mechanical restraint and high doses of drugs.

And the other thing is that we have other clients, and there are other patients all over the country that could benefit from this treatment. We have some right now who are waiting to get access to it. So those patients would lose access to have the opportunity to try this type of

treatment.

This is a safe procedure. We've used it for 24 years, 24 years at JRC. There are minor temporary limited side effects. It consistently is effective in reducing the behaviors. It's associated with a wide range of positive side effects. And it's the only treatment, after some of the less restrictive ones that are utilized, that's available to stop these harmful behaviors without chemical sedation and gives the person an opportunity to recover and improve.

This device does not present a substantial deception. As you heard before, there's a very in-depth procedure to get access to the treatment. The safety of the device is consistent with the literature. And every aspect of the use of this device is transparent. We keep so much data on the frequency of the use of this. And parents are able to come and monitor it. We send out reports regarding the number of GED applications. The person has an attorney that's there to represent them.

So this therapy does not present an unreasonable or substantial risk of harm, and any safety risks are immaterial when you really consider the full presentation of the person.

So thank you.

DR. YANG: Thank you. I would just like to thank the representatives from the Judge Rotenberg Center.

MS. CROOKES: We still will have --

DR. YANG: You have --

MS. CROOKES: Yes.

DR. YANG: Okay.

MS. CROOKES: Dr. Joseph.

DR. JOSEPH: Thank you. Hi, my name is Anthony Joseph. I'm a consulting physician at JRC. I'm being reimbursed for my time and travel here today, but I don't hold any equity interest in JRC, and I have no financial interest in the outcome of this meeting.

I went to medical school in England -- Oxford and Cambridge. I'm board certified in psychiatry. I specialize in the medication treatment of severe and treatment-refractory psychiatric patients, including those with self-injury and severe aggression, and I've treated patients like this for well over 20 years.

I've been a consulting physician/psychiatrist at JRC for about 11 or 12 years. My primary activity at JRC is to treat the patients there with psychiatric illness and psychiatric symptoms with medication.

It's important to note, I think, that medications, other forms of behavioral modification that are non-aversive and other treatment interventions that have been mentioned here today are often not effective for many patients, especially those with severe and treatment-refractory behavior disorders. The patients we're talking about here today, that Dr. Blenkush just presented, are really amongst the most treatment

refractory of the treatment refractory; so truly a specialized population.

Many more common forms of intervention frequently fail with such patients. These kinds of interventions include positive programming, psychotherapy, psychotropic medication. We often see patients who have failed on high doses of psychotropic medications and sometimes on simultaneous high doses of psychotropic medications. The term often used, of course, is polypharmacy.

These patients can often become sequestered from society, as you've heard. They can be in mental hospitals, sometimes prisons, other locked facilities. They're very often sedated with medications. Usually the sedation may reduce, to some degree, the amount of target behaviors, but that's based on sedation rather than treatment. The actual treatment component is very often ineffective.

As a side effect of this sort of treatment, patients often have difficulty learning. And I'm talking about the rehab side of psychiatry, if you will. So there's a definite impact from medication often on learning, the ability to integrate one's self into the community, and to have a sustaining relationship with families.

In such cases, treatment with a GED device is often the most effective and the least restrictive treatment that is available. GED treatment generally and frequently will reduce dangerous and self-destructive behaviors substantially and dramatically. It can work very quickly. GED treatment can

allow these patients to safely access the community, as you've seen, to have much improved relationships with their family members, and also to make progress in terms of self-care and social skills.

Based on my experience at JRC and seeing the benefits of GED treatment for many years, it's my opinion that the benefits of GED treatment generally far outweigh the risks that are either theoretical or those that might have been observed.

The benefit of helping patients who may suffer from severe self-injury, such as blinding themselves or castrating themselves, is, I think, quite obvious and far outweighs the aversive effect from skin shock. And you've heard typically how often the skin shock may be administered and the effects of that.

Also, it's important to note that in the way the terms "aversive reactions" and "side effects" are typically used in the medical community, for example, when talking about psychiatric medication, psychosurgery, ECT, compared with that realm, GED does not offer the typical level of intensity of side effect that those other forms of intervention might and frequently do offer to patients.

GED devices don't burn. And in terms of the psychiatric side effects that have been documented or observed in the peer-reviewed literature, it seems fairly clear that anxiety, depression, PTSD, and other such entities are not well supported in the literature, if they're supported at all.

Any side effects really should be reviewed, as I've already said, in comparison with the alternative treatments, if indeed there are any alternative treatments. We often talk about alternative treatments. I would like to ask you to consider that, for this group of patients, there may be alternative treatments, but that's not the same thing as saying that they are effective alternative treatments. And I think that's a very important point. And as I think probably most of the Committee members know, side effects, such as psychotropic medication and psychosurgery, can indeed have very severe side effects, including death.

Thank you.

DR. SASSAMAN: Good morning.

DR. YANG: Dr. Sassaman, as time has run down, I would ask you to limit your comments to two minutes.

DR. SASSAMAN: I will be less than that. I'm Dr. Ed Sassaman. I am a paid consultant at the JRC. I'm being paid for my time and travel here. I have no equity interest in the JRC, and I have no financial interest in the outcome of this hearing.

I went to medical school at Harvard and did my training at Children's and my fellowship at Children's in Boston. I first became aware of the JRC when Alan Crocker, who was our fellowship director, brought us there for a trip. And Alan was one of the most thoughtful and compassionate people I've ever known. He did not necessarily endorse the JRC, but he said

that that was something that we had to consider for students who were unable to be treated elsewhere.

I became more formally associated with the JRC when I was on the faculty at Brown and have been a consultant for 33 years there. I have seen students brought in in wheelchairs, ambulances, shackles, any way that one can imagine. And they have failed every treatment -- well, most major treatment programs east of the Mississippi and many west of the Mississippi. They've been on every behavior intervention that Dr. Como very adequately described this morning. They have failed. They have failed almost all medication programs.

Within days many students have been hospitalized, secondary to the adverse effects of the medication. But within weeks to months to perhaps a year, they've been able to have their scoliosis surgery repaired, their retinals reattached, their osteochondromatosis treated, their CP treated, their seizures brought under control by the consultants at Children's or the General or the Brigham, not because those consultants are any better than the physicians who followed them previously, but because they could have their behaviors treated. And the physicians who treat them attest to the use of the GED, because they feel that these individuals have the right to have their medical problems addressed.

As far as side effects, perhaps 5% of the children -- the students would have some erythema. It disappears within a few days. It might have a

freckle left as the long-term side effect. One to three percent of children have some millimeter concentric white dots around the circumference of the electrode. They disappear in two days. One to three percent of children might have a red dot, a red millimeter-sized lesion that disappears perhaps in one day. And those are the only side effects that I've ever seen.

Thank you.

DR. YANG: Thank you. So, again, I thank the representatives from the Judge Rotenberg Center for their presentations.

We'll now proceed to the brief clarifying questions. We have about 10 minutes.

Panel members, remember that we still have a Panel deliberation session this afternoon to ask questions of the JRC.

So I saw -- go ahead, Dr. Bickel, and then --

DR. BICKEL: Hi. I was wondering if you could tell me what the science is behind the stimulation parameters. How are they selected?

You know, I'm aware that the burst of stimulation is used to control the behaviors. For example, I have a neighbor of mine who used it on the dog collar to train his dog. Could you tell me the relative strength of what you do versus what was used in other procedures?

MS. CROOKES: I'm going to ask Dr. Blenkush to answer this question.

DR. BLENKUSH: Okay. So, first, as far as the strength of the

device, if you look in the literature, you're going to see a wide range of reports, and sometimes the reports are incomplete. But what I want to point out is that the devices that were used in the past, these were things like cattle prods and things that weren't necessarily designed for human use. The GED and some of the other devices, SIBIS and some of the other devices that have been used, there's a range.

First, the GED-3A, again, is 15 mA and the GED-4 is 41 mA. But remember, this is DC current, okay? SIBIS uses AC current and is about 3.9 mA, I believe. And then there are other devices that have been reported in the literature that actually have a greater output of milliamps than the GED-4. So, again, it varies. And one of the things about the GED is that the duration is two seconds. Some of the other devices, it's shorter.

DR. BICKEL: I'm asking why were those parameters selected.

DR. BLENKUSH: Oh. JRC used SIBIS in the '90s, and one of the things that happens sometimes when you use these types of devices is that there's a phenomenon of adaptation, which means that the skin shock device no longer functions as a punisher and the behaviors return. And that comes from using it over and over again, and the frequency of the behaviors accelerates and it no longer functions as a punisher, it no longer controls the behaviors.

So when that happens, then you move -- one of the things you can do is move to higher levels of stimulation. Okay. And what JRC found in

the '90s was that if you start off at a level of 15, then you're less likely to encounter that adaptation. And then we've also found that, in the rare cases where there is adaptation to the GED, we can move to the GED-4 and we generally don't see adaptation at all after that.

DR. BICKEL: I'm also interested in how is PTSD diagnosed, at what frequency with these patients who receive this treatment. And are there any sort of generalized fear reactions that they demonstrate?

DR. BLENKUSH: So, again, as I mentioned before, there are avoidance responses. Sometimes when the device is activated, the person will try to take off the device. Some people will -- they will exhibit avoidance responses, they'll try to grab the transmitter. That does happen.

But I want to point out that many of these students, many of our patients wear elastic electrodes which they can remove at any time, and many of them don't remove them. And, again, there are reports in the literature of this same phenomenon where the person is calmer and they're more relaxed when they're wearing the device and they don't ever try to take it off. And some of them even try to put it on when it's removed.

So that's some of the reports, and I don't know if -- do you want me to -- do you want to talk about PTSD?

DR. JOSEPH: Our PTSD wall is moving pretty quickly, so definitions change. But in terms of a classic case of PTSD, I'm not aware that that has been reported or experienced from this device.

DR. BICKEL: How do you assess it and what frequency?

DR. JOSEPH: There we go. I guess I'm back. Thank you.

The diagnostic would be based on observation, clinical observation and assessment of the patient.

Thank you.

DR. YANG: Dr. Weigle.

DR. WEIGLE: Hi, this is Karen Weigle.

I notice that you talked about conducting a lot of in-depth behavioral assessments, functional behavior assessments, lots of observation prior to developing your treatment plans that might include the aversive conditioning devices. What I'd like to know is if you do a full biopsychosocial evaluation. Are you also looking at medical-psychological-social aspects that may be impacting this behavior, rather than just immediate environmental impacters?

DR. BLENKUSH: Absolutely. So as far as assessment goes, let me explain all of the things that we have available. First of all, we collect frequency data on every single instance of a topography that we've defined occurs. Okay. That data is recorded by the staff hourly, and every night it's entered into a database that feeds a charting system which is based on -- which is a standard acceleration chart which is useful in displaying frequencies.

Okay. And then everything that we do in our treatment, every

single possible intervention, if it's a medication, if it's a home visit, if it's any type of intervention at all, anything that we think could potentially impact the person or have an effect on their behavior, we phase line every single event. And we can show you charts that have those phase lines on them. And the clinician can then go through and look at it. Okay, well, I changed this differential reinforcement procedure. This medication changed. We can see if the person got better or worse.

Okay. The second thing is, is that all of the staff and all of our clinicians are very involved in the care of each one of these clients. We see these people every day. We talk with their families. We read their extensive treatment histories. I mean, you can imagine that someone with these types of behavior disorders, they come in with boxes of records.

I had a patient come in recently that had thousands and thousands and thousands of pages of emergency room visits, of evaluations, of assessments, of different diagnoses, of med changes. Okay. So this is actually very typical of what we will see. So we do all of that.

And, in addition, we collect data on every single GED application. So when the GED is delivered, that information is available in the database, and I can look at that on my computer every day and see what behavior happened, what time it occurred, I can watch the actual application on DVR, and I can actually get the actual recording sheet that shows what the staff documented for that information.

And we do look at all of these other factors. I mean, I know it's not just -- you know, it's a whole person, so there's more than just immediate maintaining factors. We look at all of those other factors. But for a lot of these people, the consequences of the behavior are the most important thing to look at as far as learning how to change it.

DR. YANG: Okay. Oh, go ahead.

DR. WEIGLE: I just had one other question about tracking adverse events. Do you have like a protocol for what you're looking for with regard to adverse events? And how comprehensive is that and for how long of a time period is that used?

DR. BLENKUSH: So first, again, every person that -- the moment that they receive a GED application, every patient is put on a list to be seen by a nurse, and they go and examine the patient and look for any negative side effects.

Okay. Now again, as I mentioned before, we are very involved in every aspect of the person's life. They have a treatment team, they have a case manager, they're in a classroom, and there's a community of people who are looking after the person and looking out for their best interest.

But as far as adverse event reporting, you know, we don't really -- we collect information on their reaction. We monitor these things. But as far as like a systematic recording, I mean, there are things that we have to do. As far as anything that happens with a device, we have to report it to the

FDA. But beyond that, I mean, this is just -- this is clinical. We're assessing them as we're going along and seeing what's happening.

DR. WEIGLE: Okay, thank you. That's what I was asking about, was more of the behavioral/psychological aspects that you could possibly observe, not the physical.

DR. YANG: Mr. Mikita.

MR. MIKITA: Thank you very much.

I'd kind of like to get a better view. It seems consistent when you refer to these patients as our residents, or clients as kids and children. That's kind of not surprising in certain situations in this country. How many of your patients are indeed under the age of 18? How many people are adults over the age of 18?

MS. CROOKES: We typically consider the school-age population versus the adult population, so we break it down up until the age of 21 rather than 18. We have 100 clients who are over the age of 22 and 141 that are 10 to 21.

MR. MIKITA: Some are children and some are adults; is that correct?

MS. CROOKES: Yes.

MR. MIKITA: And some of you or all of you have testified that all alternatives have been exhausted, and then you would always walk back from that kind of universal axiomatic statement and say, well, not all

alternatives have been exhausted, just some.

So how do you determine when to use the GED devices and when "all alternatives" are really exhausted, such as the predominant therapies being used around the country being positive behavioral supports coupled with some psychotropic support? So how do you kind of piece that out? And why were you all so quick to talk about all alternatives are exhausted and then to say, well, not all alternatives are exhausted, just some, and we really know when to use this?

MS. CROOKES: I did backtrack when I said all medications. I misspoke at that point because I don't think it's possible to try all medications. However, our program is based on positive behavior supports alone the majority of the time. In those instances where the positive behavior supports, with or without medication, haven't worked, that's when we'll supplement the treatment plan with the use of the GED. And Nathan can be more specific to when that is. But we're not replacing the positive behavior supports with the aversive conditioning device. It's added to the behavior plan that includes both.

But Nathan.

DR. BLENKUSH: So yeah. I mean, I think it's fair to say that we don't try everything. It's not as if every single one of these people has had psychosurgery and ECT before they get this. That doesn't happen. We try the procedures that are the least restrictive and most likely to be effective to

address the problem behavior.

And I want to point out that the patients that come to our program, they've been in hospitals, and many of them have been on 10, 20, 30 different medications, and they've been receiving this type of treatment not just for a year or for -- they've been receiving for 10 or 15 years. They went through all of the standard procedures that any loving parent would use to try to help their child. They call experts and behavior analysis and psychology. They go to psychiatrists, who do their best to try to keep the person in the home, to try to treat the problems in the home and to reduce the frequency of the behaviors with these treatments.

But after all that stuff has been tried, they come to our program, and when they come to us, in some cases they've already done horrible things to themselves. Some of them come and they've already lost their vision, or they've mutilated parts of their body, or they have permanent side effects due to the antipsychotic medications that they've been taking.

So we typically will try a wide range of procedures again, and sometimes even medications, to try to control the behaviors and try to treat the behaviors. And usually that takes about a year before we decide to add the GED. Sometimes it's sooner. Sometimes someone comes in, and it's very clear that they've had everything else and we start the procedure sooner.

So I hope that is helpful.

MR. MIKITA: All right. And just one more question. This is kind

of an overarching question. Notwithstanding the fact that 11 states are reportedly sending individuals, through a waiver, to your program, the majority of states in this country are treating individuals that you have been treating with this device, but they are not using your device nor have they ever used your device.

So do you mean, then, that those individuals in those majority of states are not being treated effectively and not being treated in a manner that is medically indicated? Is that your belief?

DR. BLENKUSH: I would suggest that there are people all over the country right now -- they're in hospitals, they're in residential programs, they are all over, and they have received a wide range of treatments, and nothing is working for them. And that's why people are trying procedures like psychosurgery, and they're trying procedures like ECT to address these problems.

Look, this is a controversial procedure. And I understand that when you look at it from just at face value, it's controversial. And many places don't have the infrastructure in place to make this happen. JRC has a very elaborate court process. We have a way to make sure that all of the safeguards are put in place to use the device.

So, no, I do believe that there are other people out there that could benefit from this treatment, and I think that it would be great if all of them could -- some of them could get access to this treatment from other

states, yes.

DR. YANG: Thank you.

So I just want to state that we're going to be taking extra time for this because I do believe these are important questions. But in fairness to everyone that has a question, if you can keep the questions to brief clarifying questions, that would help.

So next up is Dr. Dorsey.

DR. DORSEY: Hi. Ray Dorsey.

I have questions pertaining your contentions around risks, efficacy, and questions about its application. In your materials and your discussions, you discuss that administering these shocks is "harmless" and that the risks are "theoretical." How can a device that's designed to cause harm, designed to cause pain, be harmless and have theoretical risks?

DR. BLENKUSH: Well, it's not designed to cause harm. Remember, it's designed to reduce the behaviors by applying an electrical stimulus that is sufficient enough to reduce the problem behavior. So I don't think it's designed to injure the person, and it's not designed to cause harm to the person. It's designed to treat the person's behavior disorder.

DR. DORSEY: Does the stimulus cause pain? Yes or no.

DR. BLENKUSH: Yes.

DR. DORSEY: Is pain a form of harm?

DR. BLENKUSH: Well, then that's -- I mean, if we wanted --

DR. DORSEY: Is pain a form of harm?

DR. BLENKUSH: I mean, I think it's something that people would work to avoid and something that we would rather do without, yes. So I mean, if you want to say, is it physical harm? No. But is it uncomfortable? Yeah. It's part of the process, and it's one of the things that we take into account in terms of risks and benefits.

DR. DORSEY: On to efficacy. In your publication that you co-authored, you indicate that you had 100% response rate, that all individuals responded to the contingent skin shock, and they had a 90% reduction in behaviors. Are you aware of any other psychological intervention that has 100% response rate?

DR. BLENKUSH: The GED and skin shock is not 100% effective for everybody, okay? And there are cases in the literature that show that some people it doesn't work for. And even at JRC, we've had people who have started on the GED and they've adapted to that, and we've added GED-4. And we've even seen adaptation to that in a few cases, and we've had to put in special protocols to help those particular people.

DR. DORSEY: So is the statement then on page 36, all patients experienced 90% reduction in behaviors from baseline at the end of a three-year period, false?

DR. BLENKUSH: In that study, that statement is absolutely true. But I want to also point out that that study includes 60 charts, okay, and it

shows exactly what the frequencies of those behaviors were.

Okay. So in terms of behavior disorders -- and we're talking about percent reduction -- sometimes that's not a very good measure, and it's not a good measure because if you go from 100 aggressive behaviors today to 10, you're still going to have a pretty big problem, okay? But I think if you look at those charts, you'll see that there's a range of effect. Sometimes it goes to zero very quickly and stays there. Other clients or other patients were maintaining at a different level, and it wasn't a zero level.

DR. DORSEY: Was an institutional review board obtained for the study?

DR. BLENKUSH: We went through the DDS -- IRB through the Mass DDS.

DR. DORSEY: On to application. Who places the electrodes?

DR. BLENKUSH: All of the staff that work with the patients are trained how to put the electrodes on, what to do, how to rotate them, and how to administer the applications.

DR. DORSEY: Who administers the shocks?

DR. BLENKUSH: The direct care staff that are trained to do that.

DR. DORSEY: What is the training of the staff? Are they clinicians?

DR. BLENKUSH: All of our staff receive an initial three-week

training that goes into all the different treatment components, which mostly involve positive reinforcement, data collection, instituting emergency physical restraint, and all of the policies and procedures. After a person has been at JRC for a period of time, then they can go through additional GED training and learn about the device, how to use it, and everything about it.

DR. DORSEY: Do any of the people administering the shocks, do they have medical training? Are they nurses, therapists?

DR. BLENKUSH: Well, I mean, sometimes the clinician or the nurses can be involved in the delivery of an application. But, you know, again, the clinicians design the behavioral procedures. The nurses will monitor the patients after they receive applications. But the staff that are with the patients most often are direct care staff.

DR. DORSEY: So the direct care staff who administer the shocks do not have medical training?

DR. BLENKUSH: No, they don't have medical training.

DR. YANG: Dr. Peavy.

DR. PEAVY: Guerry Peavy.

It was not clear to me exactly what ages you consider for this treatment. I thought that it might have been Ms. Crookes that said that you do not consider anybody under the age of 18.

DR. BLENKUSH: No, we don't have anyone under the age of 18. We treat people with very unique behavior problems, and I suspect that there

are clinical presentations where someone at a younger age could benefit from the use of the GED. And we have treated people that are younger than 18 with the GED. It depends on the type of behaviors the person's emitting, it depends on what treatment interventions have been used in the past, and it depends on what the risks are to the person.

DR. PEAVY: Do you have any guidelines about how young you would extend the treatment to, if they had a certain type of symptoms?

DR. BLENKUSH: I think that I don't know the youngest person that we've ever treated. Nine? Nine years old is the youngest person that's ever started on this treatment.

DR. PEAVY: Okay. So that you would still consider? That's not an old guideline? That's something you would still consider?

DR. BLENKUSH: That's the youngest person we've ever treated. So I mean, again --

DR. PEAVY: Yes.

DR. BLENKUSH: -- I can't foresee what the presentations were, but you never know what kind of problems you might encounter.

DR. PEAVY: Do you know what percentage of the patients are able to give their own consent in a valid way?

DR. BLENKUSH: So this is a substituted judgment process, and that means that the probate court judge is the person who substitutes their judgment based on all the evidence that they hear about the person's history,

about the risks and benefits of the treatment, and they have to decide what the person would choose if they were competent.

Now, I will say that we have a lot of different presentations. We have incompetent people that want to access the treatment. We have incompetent people that don't want the treatment. We have competent people who do want access to the treatment as well, and we had that in the past before, too.

DR. PEAVY: So for the people that are incompetent and do not want to access the treatment, then the procedure is to go through family or courts or both?

DR. BLENKUSH: Yes, they have a parent or a guardian. It's just like a Rogers proceeding. It's the same procedure, very similar. The person is appointed their own attorney. That person hires an outside expert. They review the treatment plan. Sometimes the plan is modified, sometimes changes are made. Sometimes there's a trial. But there's a very involved process to getting to that point.

DR. PEAVY: Just one other thing. The number of applications per week, the average is two. What is the upper -- what's the range?

DR. BLENKUSH: We have a few patients that may receive 10, 20, or 30 during some weeks. But what happens is, is that during the course of any given day, if -- I get notified whenever there's a restraint or whenever there's more than 10 GED applications, and the staff have to stop using the

device after 10, okay? They have to call me or call the attending clinician.

And then we have to go and look and see what's going on, and we have to decide, is there some reason why this person is emitting more and more problems today? Is there something wrong with the treatment? Is there something wrong with the differential reinforcement procedures? Do we have to account for other variables? And after that we might make a decision to approve them to 15. But there's a process in place to make sure that that doesn't -- yeah.

DR. PEAVY: Thank you.

DR. YANG: Dr. Reppas.

DR. REPPAS: Yes. John Reppas.

I have two procedural questions. The first is, when you formulate the treatment plan for a specific patient or client, are there specific behaviors that are selected for aversive conditioning, or does the caregiver have wide discretion about how and when they deliver the stimulus?

DR. BLENKUSH: So the staff actually have zero discretion. Every patient has a recording sheet, okay, and on that recording sheet there is each individual topography that the clinician has identified to be treated with the GED. So it might say something like aggression. Then it might say hit others, kick others, bite others. And if that's the list, okay, and that student comes in and hits somebody with an object, then the staff are not allowed to administer the GED. What they will do is call or they will write a

note and say, you know, we have this new topography that you have to include in the treatment plan, okay, or that we recommend that you do.

The clinician then has to go through an assessment, and they have to decide if that behavior should be treated with the GED, and then they will add that into the treatment plan. There's a process, there's a form that we use that goes through why we're treating it. And so there's that. And the court has to approve the individual categories that we treat behaviors for. So yeah.

DR. REPPAS: Okay, thank you; that helps. And my second question was -- you showed two anecdotal pieces of evidence around outcome, and my question is, is the person who is scoring the frequency of self-injurious events or aggressive events, is that the same caregiver who is delivering the aversive conditioning or not?

DR. BLENKUSH: It may be. Remember, these patients are receiving 24-hour-a-day care. They are monitored by staff all the time. And they're monitored by video staff as well. So their recording sheet and the data that's on it gets passed on by different staff that are trained to work with them. So there is a wide range of people that work with them and a wide range of people that mark the sheet and that administer GED applications for the person.

DR. REPPAS: But the process is not blinded, obviously.

DR. BLENKUSH: No. No, it's not.

DR. YANG: Again to the Panel, I would like to remind you, for brief clarifying questions, limit your questions to one or two. We still have nine, and I would like to -- these are important questions, so I would like to keep going on this.

So Dr. Connor.

DR. CONNOR: Jason Connor.

My brief questions are what proportion of the time, when you go to court for permission to use one of these devices, does the court deny it?

DR. BLENKUSH: Usually what happens is this, is that the person has an attorney that's representing them, and if there's a problem with the treatment plan, if the attorney or the expert objects to something, then usually what we will do is come to some decision about what we're going to do and how we're going to resolve it. Sometimes that means that the person may need a different treatment or a different trial on something else. Sometimes it means that certain behaviors won't be treated. Sometimes it means that there will be additional safeguards put in place. Like they might say, before you go to GED-4, you have to notify the patient's counsel and give them a 10-day notice before you do that. But usually we can work those things out before we actually end up in court, but sometimes they do go to trial.

DR. CONNOR: Well, maybe trial is the wrong word, but it

sounds like you mean -- my verbiage, perhaps, wasn't right. A judge has to okay each time this is introduced with a new patient.

DR. BLENKUSH: Yes.

DR. CONNOR: What proportion of the time does the judge say no, you can't on that patient?

DR. BLENKUSH: Well, we don't bring a case before a judge unless we are very sure that this --

DR. CONNOR: So is the answer zero?

DR. BLENKUSH: I don't know if it's zero. I mean, I'd have to go back and look at the records, but it's very infrequent.

DR. CONNOR: Okay.

DR. BLENKUSH: Usually we can work it out beforehand.

DR. CONNOR: That's all I was looking for.

DR. BLENKUSH: Yes.

DR. CONNOR: And then, from reading some of -- we received hundreds of pages of letters from parents and advocacy groups and such. You know, I get the idea that if someone is about to injure themselves, hit their heads, hit someone else's head, this is administered and that's what it's meant to treat. But it sounded like there were times where a student stands up in class, and presumably not necessarily with the intent to do himself or others harm, but the device is administered like for standing in class. And that was one of the complaints that I read. Is that true?

DR. BLENKUSH: Well, every single person has a unique behavior modification plan, and some of the behaviors that are treated, if you looked at them on the outside and didn't know the person's full history, you would wonder why we were treating those behaviors.

Just to give an example. The person that I was showing earlier, Samantha, her behavior -- before she came in, this is what she would do. She would bring her hands up and she would strike herself in the head, and this is the behavior that she would engage in thousands of times per day. If Samantha raises her head above her shoulder -- raises her hand above her shoulder, she gets a GED application. So in her treatment program, you're going to see a topography like "raise hand above shoulder" and you're going to think to yourself, well, why would they do that?

On the other hand, if there was a person like -- there might be other behaviors that are idiosyncratic for that person, that if we don't treat them, will interfere with that person's ability to learn, that will interfere with that person's ability to benefit from the treatment.

DR. CONNOR: And then the last one.

DR. YANG: You know, Dr. Connor, I think to be fair to the rest of them, keep your questions to one or two.

So Dr. Augustine.

We'll come back in the Panel deliberations.

DR. AUGUSTINE: Two brief questions. We talked about the

physical examination that takes place with a nurse or with an attending clinician after an application. But I'm wondering if in the last decades of use, has there ever been a time where there have been evaluations for effects that may be not visible to the naked eye -- I'm thinking about EKGs, blood work, or urinalysis -- that might give a sense of muscle injury or more detailed evaluations by a neurologist looking for neuropathy? Have those taken place?

DR. SASSAMAN: Thank you. The charge nurse at the school has actually been there longer than I have, so she knows the students and the families exceedingly well. If after a certain number of applications the staff is concerned, as Dr. Blenkush has said, she will then go down and she will take a look at the student -- or one of the other nurses -- and they will determine if indeed they are concerned that the child has -- that the student has a medical problem. Then they will seek medical intervention before the treatment continues. And indeed rarely, yes, there have been times when it's been determined that the child has an otitis, that the child might have had a urinary tract infection and that might have been contributing to the behavior. But that's extremely rare.

DR. AUGUSTINE: The question was a little bit different, sort of thinking about antipsychotics or antiepileptics or other medications where we might have periodic screenings for things that aren't necessarily evident on exam. Have there ever been times like that where, again, on a screening

basis early in the use of these, where there were EKGs, blood work, or other things looking for things that wouldn't necessarily give symptoms?

DR. SASSAMAN: That would be causing the behavior?

DR. AUGUSTINE: Not causing the behavior. Again, thinking about adverse events.

DR. SASSAMAN: Oh, okay. Sure. All of the students in the school have yearly exams. As part of that exam, they would have the appropriate medical interventions determined by the Preventive Services Task Force. Students who are on anticonvulsants have their anticonvulsant levels done either every three to six months, depending on what the neurologist at Children's or the General wants to have done. The urines are done periodically as part of their tox screens. Their liver functions would be looked at. So all of that is looked at.

DR. AUGUSTINE: Okay. A separate question. Can you just tell me a little bit about what the nature of the erythema is? So if it's not a first-degree burn, is it a contact -- what is it?

DR. SASSAMAN: Well, that's an interesting question. Is it a contact dermatitis, secondary to the nickel? Well, you might think that that would be more common. I don't know.

DR. AUGUSTINE: Is it possible that it could be a first-degree burn?

DR. SASSAMAN: I don't think so. I mean, we've had

dermatologists take a look at them, and they said no, they don't think it's a first-degree burn. It's not a first-degree burn. If you look at the effect definition on first-degree burn, no, it's not. It's an erythema that goes away, and I don't know what it is.

DR. YANG: Dr. Goodman.

DR. GOODMAN: Two questions. The first one has to do with the technical characteristics of the device. We learned earlier about -- were reminded about Ohm's Law and that current is dependent upon both voltage and resistance. You talk about delivering a certain current. I imagine it's possible to design a device so that you deliver a constant current or at least don't exceed a particular current.

Given the fact that resistance can vary between patients or within patients, could you tell me whether your device delivers a constant current and whether there's a ceiling on the current that's delivered?

DR. BLENKUSH: You know, we've had the device -- we've had engineers look at it. But your question has to do with, you know, is there an upper limit to this? There are certainly fault tolerances within the device, but as far as the amps and the RMS, there's an average RMS current which we describe and that they tested in the '90s, as far as I know. But I'd probably have to --

DR. GOODMAN: So the current that's delivered could vary?

DR. BLENKUSH: Yes, and it's a DC current, and it has a 25% duty

cycle. So the current is only on for a quarter of the time.

DR. GOODMAN: Um-hum, okay.

DR. BLENKUSH: And, again, I'd have to have the engineers talk a little more about that.

DR. GOODMAN: The second question has to do with efficacy. And this has been touched on by other panelists before. Why are you so sure of the efficacy results, either what was published in the paper or what you reported here today, in the absence of a randomized clinical trial, in the absence of randomization or sham control?

I mean, I've been fooled myself many times, thinking that a treatment that I was introducing worked, until I subjected it to a randomized controlled trial. Have you considered conducting one yourself? And this gets back also to the choice of the current, which was another question earlier on. For example, why not compare a lower amperage device to this one and see whether it really makes a difference?

It doesn't seem like there were any dose finding studies done either, which also would give you some information not only about the appropriate threshold but about whether actually you have an efficacy signal that's separate from the other aspects of the treatment environment. As you described, you don't depend upon this device alone.

DR. BLENKUSH: So the first thing is we would love to participate in a randomized controlled trial for people with the most difficult-

to-treat behavior disorders in the United States. We would love to go through and explore treatment alternatives, and we would be more than receptive to anyone that wants to do that. So that's the first question.

Now, the second thing is that, in behavior analysis, okay, which is where this technology came from, the standard types of ways of investigating the efficacy and the effects of independent variables is through single-subject design. And this comes from Murray Sidman's *Tactics of Scientific Research,* and it's about establishing a cause and effect relationship at the level of the individual subject. And you do that in a number of ways, through reversals, by putting the treatment on, removing it and then by putting it back on, and then by replication.

Okay. So in the literature, this effect has been replicated over and over and over and over again. And in clinical practice, we've seen this replicated over and over and over again, and we have had times where we've removed devices from people and we've seen the behaviors accelerate.

DR. GOODMAN: Did you present any of those data to us?

DR. BLENKUSH: As far as removal? Yes. I mean, if you look at all of the research, that's the typical experimental design that you'll see. You'll see like an AB-AB design where they show the baseline steady state performance of the self-injurious or aggressive behavior. They show what happens when the treatment is activated, and then they show what happens when you remove it and go back to baseline.

DR. GOODMAN: I just don't remember that.

DR. BLENKUSH: If you look in all the clinical research, you'll see that type of thing.

DR. YANG: Okay.

MS. CROOKES: Just to add. When we submitted the original 510(k) that was cleared in 1994, that data was submitted at the time.

DR. YANG: Thank you.

Dr. Green.

DR. GREEN: I have a question about whether the patients can identify the person who is activating the stimulus, and if so, what kind of relationship do they develop over time?

And then you mentioned that they have home visits. If they do, do they go home with the device, and if so, who would activate it then?

MS. CROOKES: Well, to answer the home visit question first, that's very individualized. There are times when they go home with a staff member if the family isn't comfortable taking the device home or if they feel as though they might need assistance from the staff. If the family is taking the device home, they also have to go through a parent training. So that's very individualized.

As far as the relationship with the device -- with the person holding the device, administering the application, and the student, we have found no adverse relationship in that. It is not blind. They're in front of the

student. We go through a verification procedure so the student is aware that the activation is coming. So none of that is hidden.

DR. YANG: Okay, Dr. Miles.

DR. MILES: You know, I'm confused here because the definition of a first-degree burn is an epithelial burn, and typically a first-degree burn lasts a couple days and then it goes away. And, furthermore, a first-degree burn can be caused by 20 mA. So I'm confused about the fact that you get red rash after you apply the electricity, it goes away in a couple days, and you don't call it a first-degree burn. Question number one.

Question number two is you all have a budget of about $60 million, which is not relevant to this hearing, but that's the size of organization that could easily sponsor prospective controlled trials. Clearly, you've been in a controversy now for a couple decades. Why haven't you done them?

Thank you.

MS. CROOKES: I'd like Dr. Sassaman to address the first-degree burn issue. But we have not published and done as much research as we had wanted because we were always in the business of treating the kids. We have offered, during this 510(k) process, to do those types of clinical studies, and we certainly are willing to do so.

But Dr. Sassaman.

DR. SASSAMAN: The dermatologists have told us that there is

no peeling, there's no sloughing, there's nothing. There's just some erythema. And so if you're saying that if you get a little bit of a sunburn and it goes away in two days, is that a first-degree burn? That's a matter of --

DR. MILES: Sloughing, as you know, is a characteristic of a second-degree burn.

DR. SASSAMAN: That's correct.

DR. MILES: Not a first-degree burn.

DR. SASSAMAN: There's just erythema. That's it. And it goes away. So is sunburn a first-degree burn?

DR. MILES: We're talking today about electrical burns.

DR. SASSAMAN: Electrical burns are the same. Indeed, that's what the -- the etiology is whether it's from sun, whether it's from current, there is erythema, and the dermatologists that I've asked this question say they can't answer it. They don't think it's a first-degree burn.

DR. MILES: Well, I'm just trying to understand your testimony before an FDA committee, that you're not seeing electrical burns when you're seeing electrical burns.

DR. SASSAMAN: Well, that depends on your definition. Is this a burn or not? I've been told that no, it's not. It's erythema. And the dermatologists say that's not a first-degree burn.

DR. YANG: All right, we better move on. So Dr. Iwata, and then we have three more after that.

DR. IWATA: It's difficult to separate questions about the device versus questions about JRC's use of the device, so that's all I can ask. I have lots of questions, but I'm just going to ask a couple by way of follow-up. One has to do with the stimulus parameters, because the questions that we're asked to address have to do with regulating stimulus parameters.

You mentioned that some clients -- patients adapt to the device, and that has required increasing the amperage of the device, correct?

DR. BLENKUSH: Yes, just moving from GED to GED-4. Yes.

DR. IWATA: My understanding of the way this whole process works is that within a given range in terms of interventions that we use, some are effective and some are not, and if they're not effective, you go on to something else. Now, electrical stimulation is designed to be very effective very quickly, which means that the individual should not experience very many stimulations, which means that very few people should habituate to the stimulus. And if they do, it's not really habituation; that is, they haven't adapted to it. It's simply ineffective, and you would move on rather than to step up the voltage, so to speak.

To use an analogy, a small amount of lemon juice on the tongue might be another aversive event, but if that doesn't work, we don't put acid on the tongue. Do you see what I mean? You just move on to something else within a typical range of stimulation.

DR. BLENKUSH: And I think that's exactly what we do. We have

our typical range of stimulation. We don't adjust the parameters of the devices. We have --

DR. IWATA: But the device went from a 3.5 mA up to a 41 mA.

DR. BLENKUSH: Um-hum.

DR. IWATA: That's quite a big step up.

DR. BLENKUSH: Yes. I mean, I can just say that I agree with what you're saying, in a sense that if you have a certain level, you want to choose the level that's going to maintain the low frequency of behaviors without them coming into contact with the stimulus. And we see that quite often.

But look, we're treating behaviors that are not -- it's not always curative; it doesn't always solve the problem forever, right? So sometimes we have to move from a lower stimulation to a higher stimulation after it's shown that it doesn't work.

DR. IWATA: But if the lower level of stimulation has been shown to be effective with a number of people, why would you just not conclude that that level is going to be ineffective or that stimulus class should be not considered and move on to something else?

DR. BLENKUSH: Well, because of the data that we get, I mean the two charts that I put up, okay, which showed a person go from hundreds and thousands of aggressive and self-injurious behaviors for a month, while they were restrained, to zero using the GED. Okay. Now, it may be that

down the line he may start to emit more self-injurious behaviors and he may come into contact with a stimulus and it may lose efficacy. But it doesn't mean that we wouldn't switch to GED-4 if we found that by doing so the behaviors went down to zero levels or low levels again.

DR. IWATA: Okay. Another question. A question was asked over here about sometimes applying the stimulus for behaviors other than self-injurious or aggressive behaviors, which are the behaviors that are of interest to this Panel, and the example was someone standing up. You gave a different example. You didn't answer that question. You gave a different example of someone striking the head. What about actually standing up?

DR. BLENKUSH: Well, we have some --

DR. IWATA: Could someone be stimulated or shocked for standing up?

DR. BLENKUSH: We have some people that have had behaviors of out of seat without permission and where they've been treated with the GED for getting out of their seat without permission. These are people, though, that when they do so, it has been a member of a chain leading to attacking somebody or other aggressive behaviors.

DR. IWATA: So the answer is they could get shocked for being out of seat?

DR. BLENKUSH: Yes, if it was for that.

DR. IWATA: Here's the next question then. For people who get

out of their seat, do you calculate the probability that getting out of seat is going to produce aggression versus getting out of seat is just going to lead to asking somebody a question or something like that? In other words, how do you know that getting out of the seat is going to produce an aggressive response when it could produce any response? Anything anyone has to do requires getting out of the seat, pretty much.

DR. BLENKUSH: The first thing we do is make sure that the person has a method to raise their hand to ask for whatever they're looking for. But the second thing is, is that this is not just -- there is an assessment process. We're looking at the individual needs of that person, and we're trying to prevent this severe aggressive behavior from occurring.

So in some cases we would look back and say, okay, here are the person's last 10 or 15 aggressive behaviors, and here's what's happened right before them. And sometimes we might use the GED to address that behavior. But as far as -- that's the process that we go through. So there is an assessment process, there is an effort to understand how often it's happening, why it's happening, and looking at the antecedents and the members of the chain that lead to the behavior.

DR. YANG: Dr. Iwata, we appreciate your line of questioning, but we must move on.

Dr. Stebbins.

DR. STEBBINS: Glenn Stebbins.

Two questions related to the requirements prior to actually implementing the treatment. The first is, what is the composition of your human rights committee? And, secondly, are there stop rules along that process? Is there a point at which -- for example, if the human rights committee says no, do you stop at that point, or do you continue to try and go through the judge and the other processes?

DR. BLENKUSH: So the human rights committee is composed of parents, of other professionals, of people from the Massachusetts DDS that come down. So there are a lot of people involved. And then there is the attending clinician who presents the case. A lot of times -- yeah.

DR. STEBBINS: Is there an ethicist on that committee?

DR. BLENKUSH: No, there's not. No. And the committee can express all kinds of concerns about what they're concerned about, if they think the plan should be approved. Sometimes members don't approve plans and there's a majority vote. So there is a process. And sometimes the clinician can take the feedback from the committee and make changes to the plan.

DR. STEBBINS: And then are there stopping rules that actually -- if you hit a no at this point, do you actually stop the process?

DR. BLENKUSH: If the human rights committee didn't approve the plan, we wouldn't be able to use the treatment.

DR. YANG: Ms. Mattivi.

MS. MATTIVI: Again going back to the questions about the stimulation parameters, in the documentation it said the FDA-approved devices were all alternating current, AC current. And yet, at what point was the decision made and why was the decision made to go to a DC?

DR. BLENKUSH: The SIBIS device was AC. And if you look at the parameters for DC current, you'll see that DC current is safer in the sense that it's less likely to cause ventricular fibrillation, it's less likely to cause all of the other problems that -- all of the sequelae that are associated with electrical stimulation. So I wasn't involved in the engineering design of the GED, but I can state that generally DC current is safer than AC current.

MS. MATTIVI: Doesn't it also require higher amperage for DC to produce a physiologic response and therefore lead more to the probability of burns?

DR. BLENKUSH: I think it's the opposite. I think that DC current is safer overall than AC current.

DR. YANG: Dr. Armstrong. Last question.

DR. ARMSTRONG: This ties into some basic behavior analysis issues. We know from animal studies, as I mentioned earlier -- going back 40 years -- that application of an aversive stimulus over time will require an increase in intensity to gain the same effect. And you are doing that and you described that you go up to a 4.

Is there a ceiling that you hit where you say that's too much,

we're not going any further, in terms of frequency and intensity?

DR. BLENKUSH: Yes. So in terms of intensity of the GED, there are only two levels. So what we've done recently is, if we do observe adaptation to the GED-4, we've actually implemented a very comprehensive alternative behavior program where the person is taught to keep their hands by their sides for people that hit themselves in the head or other behaviors. And that's been actually very effective for one patient who actually would take his hand and shove it down his throat and grab the inside of his throat and do damage inside of his throat and stick his hands in this mouth. He was taught to keep his hands at his sides now. So there are only two levels.

And the second thing is that this procedure oftentimes -- as you saw, we're able to reduce the frequency of the applications and reduce the use of the GED through skill training, through other procedures. And over time we found that even people where we thought that it would be very unlikely that they could eventually dispense with the device are able to stop using it and move on to a program that's primarily based on differential reinforcement.

DR. ARMSTRONG: Well, that's my follow-up question. In one of your slides you talked about how not having this device would lead to the reemergence of the severe problems. Is this a lifetime treatment? Are there individuals that are able to leave your facility and return to a least restrictive independent living home environment, and how often does that happen?

DR. BLENKUSH: So, first, you will hear from people that have done just exactly that. And yes, many times the combination of this treatment with a wide range of behavioral and educational procedures can help a person learn a whole new set of skills and return to typical settings, and they no longer require any GED treatment at all.

Look, we talked earlier about not completely understanding the nature of self-injury, and some of these behaviors are maintained by factors that aren't completely understood. And so for many of those patients, adding the GED can be a long-term treatment.

But remember, we're using the GED to replace treatments like antipsychotic drugs and restraint, which have side effects that are far greater in number and severity than GED. And so we look at it as every moment that someone that has these types of problems can be free of emitting these behaviors, every moment they can have to be free of restraint and free of drugs is a victory for them.

DR. YANG: All right. So obviously, due to the gravity of these issues, we have necessarily run long on this session. So lunch will obviously be delayed in order to give the Professional Societies Open Public Hearing their due time. So let's proceed to that session at this point.

Thank you again to the Judge Rotenberg presenters.

So now we'll proceed to the professional societies and organizations Open Public Hearing of this meeting. And I'll pass this to

Ms. Russell.

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

For the agencies that have provided a PowerPoint presentation, please approach the seating area by the podium when your name is called. I would also like to remind individuals that the time clock is at the top of the podium and will be displayed during your speaking time. Please watch that adequately.

The Agency has received 17 requests from professional

societies/organizations to speak prior to the final date published in the *Federal Register* notice. Each speaker will be given approximately four minutes to speak. However, one agency or organization has not signed in at the registration desk, and their name will not be called at this time.

For the record, as of April 14th, 2014, FDA has received 260 documents posted to the Docket Number FDA-2014-N-0238; 158 of those documents were posted as confidential and not to be made public.

Due to the status of our panelists who are special government employees, all of the 260 documents that were posted to the docket were submitted to the panelists for review. However, on the web you will only see 102 of those documents as of April 14th.

DR. YANG: Thank you, Ms. Russell.

As she mentioned, there are 16 professional organizations that will speak today with four minutes apiece. If you have not moved up to the first two rows or so, please do so at this time when I announce the list of organizations.

So the list of organizations includes:

1. The American Association of Intellectual and Developmental Disabilities
2. TASH: Equity, Opportunity, and Inclusion for People with Disabilities
3. Association of University Centers on Disabilities

4. Autistic Self Advocacy Network
5. Disability Rights International
6. Disability Law Center
7. National Association of State Directors of Developmental Disability Services
8. National Leadership Consortium on Developmental Disabilities at the University of Delaware
9. Queens College Regional Center for Autism Spectrum Disorders
10. The Arc of the U.S.
11. National Disability Rights Network
12. National Association of Councils on Developmental Disabilities
13. BRI Parents & Friends Association
14. Gateways: Educational and Behavioral Consultation Services
15. The ACLU
16. TASH: New England

Again, just to remind you, on the podium there is a timer, so please keep to the four minutes. We will keep you strictly to the four minutes and you'll be advised to discontinue.

There will be time to ask questions from the Panel this

afternoon after the Open Public Hearing Session Number II. So, therefore, we'll invite our first speaker from the American Association on Intellectual and Developmental Disabilities to the podium at this time.

DR. NYGREN: Members of the Committee, thank you for the opportunity to provide comments today. My name is Margaret Nygren. I'm the Executive Director of and representing the American Association on Intellectual and Developmental Disabilities (AAIDD), the oldest and largest professional society concerned with intellectual and developmental disabilities.

Class II aversive conditioning devices, which here are known as electrical stimulation devices, are designed as an intervention for challenging behaviors, those behaviors of such intensity, frequency, or duration as to threaten a person's quality of life and/or the physical safety of themselves or others.

The research simply does not support a benefit to the use of these devices for any population. There is simply very little research on the effectiveness of these devices. A review of what literature there is reveals a few case studies, retrospective record analyses, and very small subject studies. The retrospective analyses don't suggest that the intervention results in long-term behavioral change. And among the very small subject studies, it's clear that these devices are used in conjunction with other behavioral and pharmacological treatments, making it impossible to assess

the effect of the devices alone.

In short, there have been no systematically conducted, well-controlled investigations on the efficacy of these devices to address challenging behaviors.

Today, to conduct such a study would violate the ethics of virtually all clinical disciplines and the regulations administered by the HHS Office on Human Research and FDA protocols.

These devices do represent an unreasonable and substantial risk of illness or injury. These devices are explicitly intended to inflict pain. The pain is not an unfortunate risk or byproduct of the intervention. With these devices, the pain is the intervention.

The literature clearly shows that those subjected to this intervention found the experience to be psychologically harmful. Authors have reported that their subjects evidenced fear, anxiety, panic, depression, and made attempts to avoid or escape the treatment. Recent treatment recipients, when interviewed by FDA clinicians, also reported experiencing long-lasting negative psychological effects from the treatment, including nightmares, hyperarousal, anxiety, fear, depression, and flashbacks.

The JRC center itself, in a 2012 policy document, acknowledges that there are physical risks related to the device, including skin redness and small blisters. However, individuals treated with these devices have reported experiencing burns, scars, loss of sensation, and muscle contractions related

to their treatment.

There are effective interventions that do not pose a substantial risk of illness or injury. As challenging behaviors are almost certainly symptomatic of larger issues, any individuals with these behaviors need interventions that help them develop more adaptive strategies, and these devices cannot provide those outcomes.

We know from the body of empirical research that punishment-based procedures do not result in long-term reduction or elimination of such challenging behaviors. We also know from the research published in peer review journals, across all clinical and educational disciplines, that positive behavioral interventions absolutely do result in the long-term reduction or elimination of challenging behaviors.

There is no population for which these devices would be the only effective treatment or one for which the benefits outweigh the risks. While there is a large body of literature documenting a range of variation in the experience of pain and pain thresholds in human beings, there is simply no evidence that people with intellectual disability don't feel pain the way the rest of humanity does.

DR. YANG: Excuse me. Please wrap up your comments.

DR. NYGREN: Although people with autism are frequently assumed to have reduced pain sensitivity, this assumption is rooted in the communication challenges that are central to the condition. Rigorously

designed studies that have examined this issue consistently demonstrate that people with autism do display a significant behavioral reaction in response to painful stimuli, while also exhibiting difficulties in self-reporting their experience of pain.

Members of the Committee, I respectfully ask that as you consider whether to ban Class II aversive conditioning devices, that you not only ban future use of these devices but that you call for the immediate cessation of use on those people currently undergoing this treatment.

Thank you.

DR. YANG: Could I ask for the representative from TASH: Equity, Opportunity, and Inclusion for People with Disabilities?

MS. TRADER: Good morning. My name is Barb Trader, and I'm speaking today as the Executive Director of TASH, the nation's leading advocacy organization for people with severe disabilities, behavioral challenges, and support needs. TASH's advocacy positions are founded in research. Roughly 60% of our members are education and behavioral researchers. I'm also here as the chair of the Alliance for the Prevention of Restraint, Aversive Interventions and Seclusion.

On behalf of TASH and APRAIS, I urge the FDA to ban the use of electric shock devices for behavioral control for all populations.

TASH has been working toward the elimination of aversive interventions for more than 30 years. In these three decades, we've learned

that the nation's leading behavior scientists are opposed to the use of aversive interventions, as are an overwhelming number of professional groups, parent groups, and advocacy groups.

In 1990, 24 years ago, the nation's leading researchers on behavioral support for people with disabilities declared, "The routine use of procedures that deliver pain, such as shock, pinching, and slaps, procedures that result in harm, and procedures that are disrespectful or dehumanizing are no longer acceptable."

APRAIS was formed in 2004 and now numbers 29 national organizations, 26 of which are national in scope. These organizations include civil rights advocates, state agencies, education, mental health, and medical professionals, behavioral and education researchers. They also include four organizations that are led and operated by people with disabilities and nine organizations that are parent led. Together, these organizations represent well over one million members.

APRAIS' vision is clear, that all children with disabilities should grow up free from the use of aversive interventions, restraint, and seclusion to respond to or control their behavior, and free from the fear that these forms of behavior management will be used on themselves, their siblings, or their friends.

Most APRAIS members and many other national organizations have position statements against the use of aversive procedures on people

with disabilities. There are several groups here that are speaking for themselves on their position statements.

Over these past 30 years, the disability and behavioral health fields have moved aggressively away from old attitudes and beliefs that made the use of aversive behavior management strategies possible. We now view people, no matter what the extent of their disability, as fully human and people who need support, not control, in order to thrive.

Professionals and family members are working together to advance the full participation in all of what life has to offer to all people, including those with the most significant impact of disability.

The Department of Education's resource document for schools makes clear that "Any behavioral intervention must be consistent with the child's rights to be treated with dignity and to be free from abuse."

SAMHSA's National Center on Trauma-Informed Care calls for all behavioral intervention strategies to be guided by the understanding that people with behavioral challenges most likely have a history of trauma and that violent responses to behaviors are not helpful and instead make behaviors worse.

As a society, we've made great strides in disability rights over the past 30 years. As a field, we've learned how to skillfully support people with the most significant behavioral challenges.

DR. YANG: Excuse me. Please wrap up.

MS. TRADER: Therefore, it is of great importance that this Panel bans the use of these arcane and inhumane devices.

Thank you.

DR. YANG: Thank you.

Association of University Centers on Disabilities, please approach the podium.

MS. MUSHENO: Hi. My name is Kim Musheno. I'm the Director of Public Policy for the Association of University Centers on Disabilities. Thank you for providing this opportunity to comment.

The AUCD is a national nonprofit organization representing over 100 university centers that conduct research, provide education and training, and provide services to people with developmental and other disabilities. AUCD is in full support of the written comments provided by APRAIS.

And we had invited one of our public policy committee leaders to come today to testify. At the last minute he was unable, so I'm going to -- forgive me, I'm going to read his testimony. His name is Mark Smith, Resource and Family Support Coordinator at the Nebraska Center on Disabilities.

"I have worked for over 30 years with individuals with disabilities in a number of roles, including direct care provider, behavior therapist, and professional advocate as well as a family member. I currently

work as a family faculty at the University Center for Excellence in Developmental Disabilities, and similarly as part of our leadership education in neurological and developmental disabilities training programs.

"As part of my experience, I participated in returning individuals with intellectual and other developmental disabilities from institutional care to the community. The treatment these individuals received in their institutional placements included painful aversive stimuli. The individuals that I worked with who had the capacity to talk about their experiences described situations that were in no way therapeutic or beneficial. They were tortured by staff in mistaken attempts to control aberrant displays of behavior.

"One need only look at the research on aversive stimuli to note that (1) they act quickly; but (2) they are context bound; (3) the problem they were intended to address resumes once the aversive is no longer present; (4) there are data that indicate that the individual associates the aversive with the individual administering it; and (5) it can cause situations where the individual displays learned helplessness responses, that is, they stop responding in any way to avoid the aversive. In fact, the only treatment one might associate with painful aversive stimuli is avoidance. One could argue easily that it is in no way treatment in the truest sense of the term.

"The information above does not include, from my perspective, the human cost of aversive therapy. Individuals with intellectual and

developmental disabilities are historically a marginalized group within our society, shuttered away in institutions where in many cases their human needs were and are barely met. Aversive therapy exacerbates a dehumanizing environment, further indicating to the individual that they are less than those who are implementing aversive treatment, leading to conditions where these individuals are seen as less than human.

"In my experience of returning individuals to community living, I worked with dozens, if not hundreds, of individuals with extremely challenging behavior, including life-threatening self-injury, high rates of aggression, and property destruction. Aversive treatment was never employed in any of these cases, yet an overwhelming majority of these individuals not only remained but thrived in community placements through persistent positive approaches to addressing their behavior.

"We found that the more the individual could assume appropriate control over their lives, in addition to effectively communicating, the less interfering problems were observed."

DR. YANG: Excuse me. Please wrap up.

MS. MUSHENO: You bet.

"In my work, I've noted there remain proponents of aversive therapy, in particular electric shock. Based on my comments above, this is literally perplexing to me. It's not treatment. In fact, I would consider it torture and is unnecessary and should be banned as an approach to treating

severe behavior, period."

DR. YANG: Excuse me. Please stop.

MS. MUSHENO: Okay. So on behalf of Mark and the entire AUCD network, we believe that the Committee should ban the use of the GED.

Thank you.

DR. YANG: Okay, Autistic Self Advocacy Network, please approach.

MR. NE'EMAN: Good afternoon. My name is Ari Ne'eman. I'm testifying here in my role as President of the Autistic Self Advocacy Network, the leading national membership organization run by and for autistic adults and youth, ourselves. In addition, since 2010, I've served as one of President Obama's appointees to the National Council on Disability.

ASAN strongly urges the FDA to prohibit the use of aversive conditioning devices for all populations. An extensive body of research shows that youth and adults with significant behavioral challenges, including self-injury and aggression, are best served with positive non-aversive support measures. Self-injury and aggressive behavior are typically the result of lack of access to meaningful communication support systems or adequate mental health supports. Neither of these needs are met by the use of aversives.

Some have claimed that aversive conditioning devices are appropriate for a subset of children and adults who prove the most resistant

to alternative forms of treatment. As noted in the FDA research review, no evidence exists to suggest such a distinct population. In truth, those who are subject to aversive conditioning are no different than those who are served purely through non-aversive methods. I would like to address the remainder of my remarks to this particular issue.

In 2011, the State of Massachusetts, the only jurisdiction in the nation where these devices are used, prohibited the use of aversive conditioning devices for any student not currently subject to them.

In the seven months after the ban, the Judge Rotenberg Center, the only facility where these devices are used, admitted 28 new students and did not require the use of aversives to serve any of them. Are we to believe that the 81 people currently subject to these devices are the 81 most disabled and most resistant-to-treatment people in the United States of America? The suggestion is laughable.

On a personal note, had my life been different, I could have ended up at the Judge Rotenberg Center. I have the same diagnosis, Asperger syndrome, as a number of those who ended up there, subject to the devices now under review.

As a child and into young adulthood, I self-injured, I was aggressive. I was removed from my neighborhood school because of behavioral problems and elopement. If I had been born in a different place or to a different family, the years I spent graduating high school and college and

building and running an organization could have been spent subject to a treatment that the United Nations has rightly deemed torture. If I had been slightly less lucky, instead of serving as a presidential appointee and working on public policy, I could be living a life in which not a single moment would be free from the threat of pain. Luck and circumstance, not biology, make the difference.

Not every person in the Judge Rotenberg Center is like me, but every person there has someone who is like them in the broader community being successfully supported without aversives. You don't have to be able to go to college or work or even be able to talk right or type in order to live and succeed without aversives. People with severe cognitive, behavioral, and communication-related challenges are served throughout the country through positive means of support, including many with self-injurious and aggressive behaviors.

We believe the FDA should ban aversive conditioning devices in their entirety, including the removal of such devices from those currently subject to them. As evidenced by successful actions by the District of Columbia, New York State, and other jurisdictions to remove residents at the JRC to settings in which they would be served without aversives, this can be done while maintaining safe and effect service provision to the individuals in question.

The Autistic Self Advocacy Network urges the Panel not to

allow the use of aversive conditioning devices to continue with some form of labeling or device technological restriction.

DR. YANG: Excuse me. Please wrap up.

MR. NE'EMAN: Certainly. The use of these devices is unsafe for any population and in any form. Indeed, such a limited measure would be a significant step backwards, given that the devices are now currently in use at a single location. If the FDA were to allow for their use under specific circumstances, its decision would likely be utilized --

DR. YANG: Excuse me. Please stop.

MR. NE'EMAN: -- to expand the use of these devices into new locations.

Thank you very much. And we hope you take action to ban the GED.

DR. YANG: Thank you.

Disability Rights International, please approach.

MR. MATTHEWS: Hello and good afternoon. I am Eric Matthews with Disability Rights International. And thank you for your attention to this very important matter.

We are familiar, at this point, with all of the horror stories of JRC's electrical shock aversives, how children are tied down and shocked repeatedly for hours on end, how some students receive dozens of electric shocks per day, how they are forced to spend their days wearing remote

control battery packs with electrodes attached to their legs, arms, soles of their feet, fingertips, and torsos, waiting in fear for the next unannounced shock. I'd like to take a moment to speak of the gravity of these abuses under international law.

In 2010, Disability Rights International submitted an urgent appeal to the United Nations, which presented evidence that the use of shock devices at JRC constitutes nothing less than torture. Two subsequent UN Special Rapporteurs on Torture agreed with us that the abuses rise to the level of torture under international law, and both have asked the United States State Department to investigate JRC. This request was forwarded to the Justice Department and an investigation is ongoing.

After reviewing DRI's report about JRC's shock regime, the UN's top expert on torture, Manfred Nowak, declared, "Yes, I have no doubts about it. It is inflicted in a situation where a victim is powerless. And a child in the restraint chair, being then subjected to electric shocks, how more powerless can you be?" The severe pain inflicted cannot be rationalized. Says Nowak, "The prohibition of torture is absolute."

The issue is broader than JRC, as stressed by Nowak's successor at the UN, Juan Méndez, current Special Rapporteur on Torture, who states that any use of electricity on a person's body raises the question of "whether it inflicts pain and suffering tantamount to torture in violation of international law."

Governor Deval Patrick and Massachusetts' Department of Developmental Services have considered this and revised state regulations in 2011 to prohibit shock in future treatment plans at JRC. But children previously admitted to the facility continue to receive shocks. There is the further risk of other programs shocking children in other states, or even JRC relocating, as they have done twice in the past, in order to avoid local regulations.

In examining JRC, it is important for the FDA to not just consider the unapproved modifications to their shock devices, but to ban the use of all electric shock devices for aversive treatment.

To reiterate the horror of how liberally these shocks can be used at JRC, an investigation by New York officials found that children can be shocked for as little as nagging, swearing, or failing to maintain a "neat appearance."

To quote Greg Miller, a former teacher's aide at JRC, "A kid drinks out of a paper cup and finishes his water and then carries the paper cup. You have to shock the student for tearing that paper cup, the same as if they tore something off the wall. This is torture."

Disability Rights International urges the FDA to come down on the right side of history and on the right side of international law and to put an end to the torture of children with disabilities in the United States.

I will end with a quote from Secretary of State John Kerry

regarding electric shocks at JRC. "This is an inhumane form of discipline, and I'm particularly troubled by it, when positive behavioral supports have been so successful. I understand that there are ongoing state and federal investigations, and I hope they result in an end to this archaic practice."

We urge the FDA to ban the use of aversive devices -- for aversive shock devices.

Thank you very much.

DR. YANG: Thank you.

Disability Law Center.

MR. GLASSMAN: Good afternoon. My name is Rick Glassman. I'm the Director of Advocacy at the Disability Law Center in Boston. We're a nonprofit legal advocacy organization that also functions as the protection and advocacy system for Massachusetts. That means we have a mandate under federal law to protect people with disabilities in Massachusetts from abuse and neglect and to assist in educating policymakers.

I'm going to speak briefly about issues related to safety, risk of injury, and emotional trauma specifically connected to the strength of electric shock. And the most important thing I think I can say is to urge you to read an affidavit that's attached to the written comments that I submitted. It's by Dr. James Eason.

Dr. Eason is a researcher at Cal Poly who was retained by us. He's a biomedical engineer and holds a Ph.D. in biomedical engineering. He

specializes in the physical effects of electric shock on the human body. And consulting for DLC, we asked him to review the GED-1, GED-3A and 4, and he found that these electric shock devices may present a substantial risk of injury, especially given their higher levels of strength.

And I would like to, before moving into some of Dr. Eason's comments, just mention, I think, the importance of the problem that the Panel has in the way this issue has been posed. We have a very scholarly and thorough presentation by the FDA that focuses often on the historic devices because those are the ones that have been cleared.

Paradoxically, the devices that are actually being used are ones that have not been cleared or approved. We understand the need to look at all of these devices. That's part of the questions that have been posed to you. But we would urge the Panel to take a particularly practical approach in looking at the strength of the devices that are being used, because they have unique characteristics and they're particularly troubling.

If you take a look at this slide, it's based on Dr. Eason's affidavit, and it shows the relative strength of common devices. The dog training collar -- Dr. Bickel's question -- is it two to four for peak current. Electric fence. Four milliamperes for the typical electric fence. The SIBIS would be peak current of 10 mA. And the self-reported pain thresholds, based on research that's is identified by Dr. Eason, is 1 to 10 or 10 to 50. And then you see the GED is at 30 and the GED-4 is at 90 mA for peak current.

The GED is about three to four times the strength of SIBIS, and the GED-4 is about three times the strength of the GED-1.

Now, this is a chart that I think, as Dr. Bowsher's presentation indicates, is somewhat simplified. It doesn't address issues -- it can't address issues like placement of electrodes or whatever. But simply looking at the differences between these devices in peak current helps explain one component of why Dr. Eason found that these devices can create an extreme level of pain, sometimes nerve damage, muscle cramps, soreness, skin and so forth -- skin injuries -- and why they could also result in emotional trauma, symptoms of anxiety, depression, and so forth.

I would particularly urge you to give careful attention to testimony we're going to receive from former employees -- one former employee and two former residents, one by video and one in person. And I think those individuals are going to help underscore, from personal experience, the pain levels, the physical effects, and the emotional trauma.

And with that, I thank you for the opportunity to comment and hope that you will decide to ban these devices.

DR. YANG: Thank you.

National Association of State Directors of Developmental Disability Services.

MS. THALER: Thank you and good afternoon. My name is Nancy Thaler, and I am testifying in my role as the Executive Director of the

National Association of State Directors of Developmental Disability Services. The association represents the nation's managers of publicly funded service systems for people with intellectual and developmental disabilities in 50 states and the District of Columbia.

On behalf of the association's board of directors and members, I urge the FDA to ban the use of electric shock for behavior modification.

The directors of state IDD agencies are responsible for providing services to more than one million children and adults with IDD, including individuals who exhibit severe self-abuse, assaultive behavior, and even individuals who have been accused of and convicted of crimes. The directors of the state IDD agencies see no need for aversive behavioral interventions.

Both science and policy have evolved since the introduction of aversive interventions decades ago. Today, the vast majority of state agencies have prohibited the use of interventions that deliver pain, deprive people of their rights, and are dehumanizing.

Understanding how the brain works and that behavior is frequently an indication of a troubling condition such as physical pain, stress, or trauma, states have altered the approaches they use to serve people with challenged behaviors. Rather than restricting or forcing a change in behavior, states see it as their responsibility to understand the person's needs and design supportive interventions such as assuring a trauma-free environment,

providing treatment for post-traumatic stress and other mental health diagnoses, teaching communication, and making sure that each person has relationships and a meaningful life.

Forty state agencies and the District of Columbia have adopted regulations and policies that expressly prohibit the use of interventions that cause pain, are humiliating, and violate human rights.

As an example, the District of Columbia, which has successfully brought individuals who had been at the Judge Rotenberg Center back to their home and community where they are receiving services without the application of painful treatments or punishments, has adopted regulations that expressly prohibit any procedure or action that is degrading, humiliating, harsh, punitive, painful, abusive, that causes unique undue trauma or deprivation of rights, that is used as a means of coercion, discipline, or retaliation, and the aversive procedures defined as unpleasant, painful, uncomfortable, or distasteful stimuli used to alter a person's behavior. The use of aversives in the District is strictly prohibited in all programs funded or operated, including, but not limited to, shock therapy, white noise, and bitter-tasting food procedures.

Of the remaining 10 states that have not yet adopted such policies, the directors in a majority of those states are on record as refusing to approve strategies that cause pain, humiliate, or violate human rights.

The progressive policies and practices of state IDD agencies

provide evidence that interventions that cause pain are not only wrong but are unnecessary, and that alternative strategies are available and are in use on a large scale.

Thank you for your attention to the matter and the opportunity to provide comment.

DR. YANG: Thank you.

National Leadership Consortium on Developmental Disabilities at the University of Delaware.

MS. WEISS: Good afternoon. My name is Nancy Weiss. I'm speaking on behalf of the National Leadership Consortium on Developmental Disabilities, a consortium of 11 national disability organizations.

The Judge Rotenberg Center claims that electric shock is used only for self-mutilating or other threatening behaviors, but it's clear that this isn't the case. A New York State report found that students were shocked for such harmless behavior as stopping work for more than 10 seconds, interrupting others, whispering, and slouching.

One young woman, who is nonverbal and has a severe cognitive disability and is blind, was shocked repeatedly over months for moaning and attempting to hold staff's hand. She was later discovered to have a cracked tooth. Her attempts to communicate pain were punished.

People have been shocked for toileting accidents, even after politely raising their hands to ask for permission to go to the bathroom for

over two hours.

The *New York Times* quotes James Eason, Professor of Biomedical Engineering at Washington and Lee University, as saying, "The lowest shock given by Rotenberg is roughly twice what pain researchers have said is tolerable for most humans."

The former director of the center testified at a Massachusetts legislative hearing that one student received 5,300 shocks in one day. In this testimony, he stated that over a 24-hour period, this student, a teenager who weighed only 52 pounds, was strapped to a board and subjected to an average of one shock every 16 seconds.

The GED malfunctions with regularity and delivers what the center calls spontaneous activations. A *Mother Jones* article quotes a JRC report that reads, "Jamie Z. was getting his battery changed; Louie G. received a shock. A former student reports being shocked in error dozens of times, sometimes when the shock was meant for another student or when the device malfunctioned and began to give shock after shock after shock, until staff could get to her backpack and disconnect the wires."

The FDA's Executive Summary describes a well-publicized incident during which staff at a Judge Rotenberg Center group home received a call from a person who said he was a quality control monitor. Staff were told to awaken two residents, strap them to restraint boards, and shock them. One resident was shocked 77 times and the other 29 times. Later, it

was discovered that the call was a hoax perpetrated by a former student. An important consideration about this hoax -- it resulted in innocent students being shocked 106 times in error -- is that staff didn't question the request to wake people up in the middle of the night and shock them for something they ostensibly did earlier that day. It's common practice and counter to accepted behavior modification intervention.

One former student says that she pleaded with staff during her early weeks on the device to tell her what she was not allowed to do, for what would she be shocked, and the staff just laughed and said, you'll figure it out. One student described life at Judge Rotenberg Center as a life lived in constant mortal fear.

There are not protections for people at the Judge Rotenberg Center. While the use of shock is court approved, it is a rubber-stamp process. In years of tracking the probate court approval process, we have found not even one case in which JRC's request to use electric shock was denied. The person has no meaningful representation, and there's no informed consent or opportunity to refuse treatment.

Parents are not informed about what their son or daughter is being shocked for or how frequent or painful the shocks are. For JRC to accept students, parents have been forced to give up their guardianship of their sons or daughters, and then when they find out what's being done to their children, they cannot get them out without spending thousands of

dollars to go back to court to regain guardianship.

We urge you to ban these devices. People across the country with behaviors just as severe -- in fact, hundreds of people who used to be at JRC and left before the facility felt they were ready -- are being served successfully in every state across the country.

DR. YANG: Excuse me. Please wrap up.

MS. WEISS: I will end with a quote from David Coulter, a neurologist at Children's Hospital, who states, "In 28" --

DR. YANG: I'm sorry. Thank you.

Queens College Regional Center for Autism Spectrum Disorders.

DR. BROWN: Hi. My name is Dr. Fredda Brown. I am a professor at Queens College, and my work has been focusing on the educational and behavioral support for students and individuals with severe disabilities, especially in the area of challenging behaviors. I have published several books, many chapters in books, and many peer-reviewed articles. And I have been in this area for 40-plus years, starting in 1973 at Creedmoor State Hospital in New York, where I used aversive interventions such as ammonia, sniffing ammonia, foul taste in mouths, and so on. I did not use contingent electric shock, however, and I do not use or support the use of any of this at this time. But this has led me to consider how treatment perceptibility changes across time.

So treatment acceptability is one's perception and judgment regarding whether the procedures proposed for treatment are appropriate, fair, and reasonable. And just what should be considered acceptable or not acceptable treatment is one of the really major issues of why we're all here today.

I have written that scientific evidence for an intervention must be balanced with its social validity, that is, treatment acceptability of the intervention. So we need both scientific evidence and treatment acceptability, and both must be met for our field to incorporate it into our menu of best practices.

I have here some data that should actually look familiar after some of the data presented today. What I did was I took the evidence-based practice website, which had over 100-plus articles saying that they supported contingent electric shock, and I took out those that were not peer reviewed, or at least in the '60s did not appear to be peer reviewed, and obviously we see a major decrease in research on shock across time.

I did put in a phase-change line in around 1990 to show where the availability of positive alternatives became very abundant in our field, and actually just recently saw a type of meta-analysis by Beaver and Iwata on functional analysis and that progression across time. And it actually would be the inverse of this. As that grew, we saw research in this type of intervention decreasing.

And then in the 1960s, early on -- in the left side of this graph -- we have to consider that we were a new field at the time and we reveled in our ability to control people and to control behavior. And I don't think, however, that we were really looking at people as people then, as evidenced in article titles such as "Reducing Rocking Behavior in Retardates," or "Reducing XYZ in Mongoloids." Obviously, this is not just a language change that has occurred, but all of our educational and behavioral technology has occurred, making these types of early articles inappropriate to consider.

And my next slide is based on -- it's an excerpt of some research that I've done looking at changes in treatment acceptability across time. And what we found -- this graph shows people, professionals, ABA professionals and PBS professionals who had once used contingent electric shock or other types -- sensory punishment or physical punishment such as hitting a child or restraint for punishment or electric shock -- when they chose to stop using it. And, again, it's interesting to look at it in the '90s. So people are stopping using these kinds of interventions.

DR. YANG: Excuse me. Please wrap up.

DR. BROWN: Okay. So what I want to say is if we extend this line, we can wait for the continued evolution of our field and maybe we will one day reach zero. But in the meantime, if that's 20 years from now, we will continue to have individuals who are bruised and shocked.

DR. YANG: Excuse me. Please stop.

DR. BROWN: I have 10 seconds.

LCDR RUSSELL: No, you went over.

(Laughter.)

DR. YANG: Okay, the Arc of the U.S.

We are strict.

MS. FITZGERALD: Good afternoon. My name is Maureen Fitzgerald. I am the Director of Disability Rights at the Arc of the United States.

The Arc is the largest community-based organization for people with intellectual and developmental disabilities. We have over 700 state and local chapters across the country. We've been devoted to promoting and protecting the human and civil rights of individuals with intellectual and developmental disabilities for over 60 years. For over 30 years, the Arc has had position statements opposing the use of aversive practices that are intended to change individuals' behaviors. We have a long history of promoting positive practices.

Our current position statement that was adopted in 2010, along with the American Association on Individuals with Intellectual Disabilities, states that research indicates that aversive procedures do not reduce challenging behaviors, and in fact can inhibit the development of appropriate skills and behaviors. These practices are dangerous, dehumanizing, result in the loss of dignity, and are unacceptable in a civilized

society. The Arc and AAIDD are opposed to all aversive procedures such as electric shock.

Interventions must not withhold essential food and drink, cause physical and/or psychological pain, or result in humiliation or discomfort. It's anathema to the Arc that any program would use practices that hurt, degrade, scare, or threaten an individual into being compliant. These practices devalue human life and are abhorrent to the individuals with disabilities, their families, professionals, and interested people who comprise the Arc.

We've been a leader in changing the practices in large congregate facilities and in pioneering the use of community-based alternatives for individuals. We've always been guided by the values of seeing people for their dignity and their worth as human beings. We've always built programs that ensure quality and safety.

Our philosophy is one of modeling techniques for individuals so that they can develop appropriate behaviors to substitute for challenging behaviors. We do not advocate using punishment techniques to deter individuals from challenging behaviors.

Our overarching goals are to ensure that people have all of the supports they need in order to fully participate in society and have the same rights and protections as every other member of society, including freedom from harm and abuse.

We believe it's the responsibility of government to protect people from abusive practices. We think that the FDA has an ethical and a moral responsibility to ban the use of devices that emit electric shock to punish behaviors that are related to individuals' disabilities. We urge you to ban the use of the GED and any other devices that use electrical current to modify individuals' behaviors.

The GED is used in the guise of treatment. It is actually punishment. Using aversive procedures to change behaviors of individuals with intellectual and developmental disabilities is dangerous, dehumanizing, it's a violation of civil rights, it results in the loss of dignity, and is unacceptable in a civilized society.

Thank you

DR. YANG: Thank you.

Next is National Association of Councils on Developmental Disabilities.

MS. GRANT: Thank you to the Committee members for giving me the opportunity to speak here today. My name is Esme Grant, and I'm the Director of Public Policy for the National Association of Councils on Developmental Disabilities.

NACDD represents the 56 governor-appointed councils on developmental disabilities in every state and territory of this nation. The DD councils are authorized under the Developmental Disabilities Assistance and

Bill of Rights Act, or the DD Act, to advise on the best interests of people with developmental disabilities and to serve a key role as creators of programs and services that help fully integrate people with developmental disabilities into their communities. Importantly, the DD councils are made up of a majority of people with disabilities and their family members, such as myself.

The DD councils asked for the National Association to be here today to not only urge but to implore that the Food and Drug Administration ban the inhumane and unnecessary use of aversive conditioning devices.

Earlier this fall, NACDD joined its members at the White House to celebrate the 50th anniversary of the DD Act, the federal legislation which the DD councils are charged to uphold. This legislation clearly delineates that the federal government and the states have a joint obligation to ensure that public funds are provided only to programs serving individuals with disabilities that meet minimum standards relating to services free of abuse, neglect, and violation of human rights.

The use of aversive intervention contradicts this historical legislation. It also disregards the Individuals with Disabilities Education Act's (IDEA) clear preference for positive behavioral interventions. IDEA, the main federal legislation regulating education of children with disabilities, strongly supports the commonly accepted preference for positive behavioral intervention supports. The federal position is clear on this matter, and a ban on aversive conditioning devices would be consistent with federal policy.

Aversive procedures are not consistent with practical approaches or best practices in addressing the behavioral needs of students with disabilities. Behavioral supports should be person centered, individually designed, positive, culturally appropriate, and allow for modifying or replacing the environment.

There is significant research documenting that aversive procedures are not effective long-term methods for reducing challenging behaviors. The use of aversive treatment can also result in the unintended consequence of hindering the development of the very skills and behaviors necessary for counter-aggression and self-injury.

Our DD councils throughout the country have supported successful programs that provide positive behavioral plans, occupational plans, and techniques for positive communication.

This year the federal government has released, through the Department of Health and Human Services, sweeping new regulations on how federal funds can and cannot be used in home- and community-based services. Further, we are seeing some of the most powerful Olmstead settlements ensuring that states are treating people with disabilities with the full dignity and respect of all other human beings, as assured under the Americans with Disabilities Act. We are just in the wake of new regulations under the Rehabilitation Act of 1973, that businesses receiving federal contracts must employ people with disabilities in their workforce.

This year has shown that the federal government can and will enforce the rights of people with disabilities, and it will go to the extent of the law and our constitution to ensure that every American has the same rights to freedom, liberty, and pursuit of happiness. The use of aversive conditioning devices such as those used at the Judge Rotenberg Center are inhumane, unnecessary, and deprive these children and adults of their constitutional freedoms.

The DD councils are also concerned about profits being made at the expense of harmful treatment of children and adults with developmental disabilities, as revealed by major national and local media.

DR. YANG: Excuse me. Please wrap up.

MS. GRANT: Thus, NACDD respectfully requests that the Food and Drug Administration take a firm stand today and ban these devices so future generations will not have to endure this detrimental treatment.

Thank you very much.

DR. YANG: Thank you.

BRI Parents and Friends Association, please come to the podium.

MS. GOLDBERG: I'm here today representing BRI Parents and Friends Association, which consists of parents, siblings, and guardians of those attending the Judge Rotenberg Center.

For years our children have severely injured themselves, us,

and others. We try to protect their heads, their eyes from damage, tried to keep them from biting, pulling hair, hurting siblings, breaking furniture, and putting everyone around them in danger. We saw them held down for hours at other schools, put in timeout rooms with no chance to learn. Our children were in and out of psych hospitals, as doctors tried different combinations of powerful medicines. All of these treatments were ineffective. Our families went through physical and emotional torture, and that is why we are the strongest supporters of the GED devices.

My son, Andrew, has been effectively treated with the GED device. He is no longer the aggressive teenager sending staff to the hospital once a week or more. He is not restrained on the floor for hours or strapped to a papoose board. He is no longer drugged into a stupor, drooling and sleeping most of the day, yet somehow still being dangerously aggressive. Andrew is awake, he's happy, he's alert, he's a person with dignity. He puts smiles on everyone's faces. And he takes no behavior-altering drugs. For those who say the GED is abusive, I wish they could see my son. It was the key to changing his behavior.

Our families feel that GED devices are the most humane treatment for our children who suffer severe behavioral disorders. The skin shock is quick and effective. It is used for specific targeted behaviors when prompts do not stop the dangerous or self-abusive behavior. It is safe, with controls followed before and after. By stopping the behaviors, our children

can then be taught acceptable behaviors and heavily rewarded for using them. You can't learn new behaviors when you're on the floor, heavily drugged, or sitting in a timeout room.

Our children are now functioning at their best. They're learning academics, going to the workshop, they have jobs, but most importantly, they can be part of our families again. They come home for visits. We cheer for them at Special Olympics. They go to the movies. I volunteer on the human rights committee, and I see those who graduate from the GED device. They lead productive lives and have made exciting progress.

Talking to other families, I hear words like miraculous, amazing, we are blessed to have the GED help our son or daughter. I feel my son has been given a second chance at life. We are thankful and feel it would be irresponsible if the GED devices were not available to those who need them. Our families know that when these devices are used with a positive behavior program, they provide the most effective treatment for our unique children. We love them, we love their new life, and we will fight to keep this treatment.

Thank you.

DR. YANG: Thank you.

Gateways: Educational and Behavioral Consultation Services, please.

DR. OLIVA: I am Dr. Christopher Oliva, a senior educational and

behavioral consultant with Gateways: Educational and Behavioral Consultation Services in New York.

I entered the field of applied behavioral analysis in 1973, working with Project Exodus, the name of the program administering the re-institutionalization of Willowbrook residents to their home boroughs in the city of New York. In these early days of behavior modification, we used a strict reward and punishment paradigm with not much in between, and we used a fair amount of punishment.

From there I joined the staff of the Kansas Neurological Institute and earned my doctoral degree from the behavioral capital of the world, which was the University of Kansas at the time.

Specific to our purpose today, I have viewed the use of contingent electric skin shock -- and I'll be saying that instead of devices -- from a variety of perspectives. These include as a member of human rights committees, a peer review committee, as a clinical director, an executive director, graduate university faculty, educational and behavioral consultant to families, schools, agencies, state government, and as a panelist to the New York State child exception panel.

Each child from New York State that will be subjected to that -- there is an application made for them to be subjected to aversive treatment -- must go through a panel, an 18-member panel, and the panel reviews -- and a subset of the panel reviews and makes recommendations to the

districts about whether these should be approved or not.

In these roles, I have worked with and had knowledge of persons before, during, and after contingent electric skin shock treatment. There are many more examples of how I personally worked with people who were en route for contingent electric skin shock, but my experience had informed my clinical practice and strengthened my interest in constructive, educative, and function-based procedures. As a member of the child-specific exception panel, my thoughts were reinforced after six years of reviewing applications.

Certain themes emerged. One, no FDA. Going for aversives, no FDA. Or many times, if there was an FDA, it would be inadequate to formulate a behavior intervention plan. The behavior intervention plans had little or no relationship to the functions of behavior. And that is under IDEA and New York State guidelines; that's a requirement of law.

The use of contingent electric shock on non-aggressive and/or non-dangerous behaviors was regularly experienced. Little or no attempt to prevent the problem behavior from occurring or deliberate provocation of the behavior was apparent. There was a use of precursor behavior, shocking precursor behaviors that were not dangerous or self-injurious, and there was a lack of range of evidence-based positive interventions consistently employed over time.

And I know the panel -- we had a discussion about that today.

The panel generally did not have a problem deciding that one or two procedures were not enough. And they weren't. And then, when in fact there were function-based procedures included in the plan, they were not done in the way that might be most efficacious. There was also an over-reliance on consequence-based treatment. So prevention was not part of it very much.

DR. YANG: Excuse me. Please wrap up.

DR. OLIVA: And behaviors for which contingent electric skin shock were used are the same types of behaviors that are successfully addressed across the country every day. The same behaviors.

Thank you.

DR. YANG: Thank you.

ACLU, please.

MS. BELLAMY: Thank you, distinguished Committee, for holding this important hearing. My name is Jennifer Bellamy. I'm a legislative counsel from the American Civil Liberties Union, and the American Civil Liberties Union would like to urge you to ban the use of noxious electrical stimulus as a behavior modification tool.

For the FDA to ban a device, it must find that the device creates an unreasonable and substantial risk of injury or that the device is presented with substantial deception. The GED meets both criteria. The GED is intended to cause pain. That is the aversive method of achieving compliance.

But the voltage is also sufficient to cause burns on skin. Over time, electric shocks may cause the scarring of skin, hair loss, tooth damage, and impotence. Most importantly, the GED causes emotional and psychological harm.

The New York State Education Department's report found that as a consequence of JRC's aversive techniques, many of the students they spoke with were suicidal and that fear, anxiety, and widespread loneliness were pervasive among the students they interviewed. Letters and interviews with former residents at JRC testify to the physical and emotional harm of the GED.

Finally, both the Mental Disability Rights International and the United Nations Special Rapporteur on Torture have found the use of the GED to qualify as torture.

The Judge Rotenberg Center maintains that the use of the GED and aversive therapy are necessary to prevent self-harm. But reports from staff, former residents of JRC, and JRC's own data show that shocks are administered in response to any undesirable behavior. From leaving a chair, to stopping work for 10 seconds, to flapping one's hands, to slouching in a chair, to not taking off a coat, none of these behaviors are self-injurious.

The JRC center describes the shock of the GED as if it were a two-second bee sting. Former residents dispute that characterization. Significantly, the JRC does not allow the public journalists or anyone in the

public domain to try the most powerful GED-4. A staff member will demonstrate the GED-1 but not the stronger GED-4.

In a lengthy review of JRC's online material, none indicate the frequency randomness at which the aversive electrical shocks are used. None of the materials include a video of a student being shocked. None of the materials show the four-point restraints used to hold students in place while being repeatedly shocked. Unless the JRC makes such details clear in its conversations and presentations to parents and judges, it seems fair to conclude that JRC engages in significant deception towards those who must approve the use of the GED.

The use of noxious electrical stimulus subjects individuals with disabilities to treatment that is different from students without disabilities, treatment that is worse than students without disabilities, treatment that is painful, dehumanizing, and random. In short, these students with disabilities experience discrimination solely by reason of their disability, which is in violation of the Americans with Disabilities Act.

JRC staff has argued that their aversive methods are effective. However, the ACLU maintains that the efficacy of the GED is irrelevant. The use of noxious electrical stimulus is inhumane. The fact that we consider using it on people with disabilities, and only people with disability, is evidence of significant bias and discrimination. We urge you to ban the use of these devices.

Thank you for holding this important hearing.

DR. YANG: Thank you.

Our last speaker is from TASH: New England.

What is your --

MR. DECKER: National Disability Rights Network.

DR. YANG: Okay, we'll come back to you. We'll let you finish.

Go ahead, TASH.

MS. BROWN: Thank you very much for holding this hearing. I really appreciate the opportunity to speak today. My name is Lydia Brown, and I am a member of the board of directors of TASH: New England. I'm one of two of our board members present here today. I would like to speak about the substantially deceptive nature of contingent electric shock and how that is inherently and inextricably tied to the substantial risk of injury posed by devices that are used to administer contingent electric shock.

All claims in support of contingent electric shock, we believe, are substantially deceptive for a number of reasons, one of those being that, as has been discussed numerous times by a number of the other representatives here today, that contingent electric shock as a mode of treatment for challenging and severe behaviors is severely outdated. It has been roundly rejected in the field of treating severely aggressive or self-injurious behaviors.

In 1990, as you heard earlier, a group of leading researchers in

the field of treating people with significant disabilities, who have the most severely harmful and aggressive behaviors, were strongly condemning all aversives as painful, damaging, and dehumanizing.

Following that, in 1993, Ivar Lovaas, who was actually the pioneer of the use of contingent electric shock as a treatment on autistic people, also repudiated the use of aversives, recognizing that even his own prior work, as you heard from a few people here today as well, was no longer representative of what should be considered as acceptable treatment or what should be considered as effective treatment.

The professional literature and practice do offer alternatives to contingent electric shock. As you've already heard from representatives today, people who have the very same severely self-injurious and aggressive and violent behavior as those who are said to be the ones that need the treatment of the GED are successfully treated in other treatment settings using non-aversive, non-punitive methods of positive behavioral interventions and support.

There is a very robust array of peer-reviewed literature and practice supporting a variety of functional behavior interventions that emphasize positive supports, that emphasize communication, and that emphasize respecting the dignity and right to self-determination of the individual receiving the treatment.

The only institution who you heard from today, the Judge

Rotenberg Center, that does use contingent electric shock is substantially deceptive about the way that they use their own device. They make the claim that the device does not cause harm. However, their device does cause harm, both physically and emotionally. It causes long-lasting effects, retraumatization for those who have been prior survivors of trauma, for whom that trauma will be re-exacerbated by the setting in which they are placed. It causes issues such as burns, which have been documented both in an NYSED investigation report from 2006, as well as in other documents.

The GED also has the potential to trigger other neurological injuries, for example, seizures, which are a fairly common feature in a number of people with intellectual and developmental disabilities, particularly among the autistic population, which represents a significant portion of the people who are served at the JRC. And the risk of that injury is not merely substantial, but it is also outright unreasonable.

Considering that there exists so many evidence-based treatments, in policy and in practice, for the very same behaviors, then there's absolutely no reason whatsoever that contingent electric shock should continue to be permitted for use in this day and in this age.

The fact that people are subjected to these interventions, in violation of their right to have fully informed consent and the right to be afforded full due process in order to determine what treatments will utilize the principles of self-determination and community living, is further

abhorrent when we have so much theory and practice supporting much more humane treatments for all people with disabilities.

DR. YANG: Excuse me. Please wrap up.

MS. BROWN: We ask that you ban the use of all devices that are currently in use, devices that have been approved that are not in use any more, and devices that may have been proposed --

DR. YANG: And now our last speaker from the National Disability Rights Network. Please accept my apologies for missing you on first pass.

MR. DECKER: Yes, that's okay. Actually, maybe the Committee should have borrowed a device from JRC to help control loquacious speakers today who could probably use a little behavior modification.

I'm Curtis Decker. I'm the Executive Director of the National Disability Rights Network. We are the association of 57 protection and advocacy programs. We provide legally based advocacy services to the full range of people with disabilities. You heard from one of our affiliates in Boston, the Disability Law Center, and we associate our comments with Rick Glassman and the work they've been doing on this issue for so many years.

You've heard from multiple speakers of the range of positions where people have decided to take an adverse position to aversive therapy and also the change in the clinical approach to this. But I want to take a

slightly different tack and just give you a sense of what I consider the voracious appetite that still exists throughout the country to use seclusion, restraint, and aversive therapy for people with a range of disabilities.

As you heard, 11 states send children to JRC until this day. Some of those states actually banned the use of aversives, and the state uses JRC as a way of being able to avoid the ban in their states that many of the advocates in this room have tried to establish over the years.

Our own association has issued two reports of the use of seclusion and restraint throughout the country. It is something that happens in every state. And in our attempts in Congress recently to try to ban the use of seclusion and restraint, we saw a letter from the Association of School Administrators saying that they could not function, they could not maintain order in their schools if they didn't have the ability to use seclusion and restraint.

So this is an epidemic in this country, and I want you to think about the implications of how this device and others could expand if the FDA does not ban this device.

I think the other thing I heard today in the testimony from the research director of JRC, I took that to be actually a blurb from their new brochure on how to market this device throughout the country. He said, if you remember, that there are so many kids -- so many children and adults around the country who would benefit from this device and unfortunately

they can't get access to it.

So I would consider the fact that while we make a great deal about the fact that JRC is at the moment the only institution using this facility, without the ban of this device, I think you'll see a proliferation of this kind of technique throughout the country, and as I said, because there seems to be a sense in so much of the provider community that they need this device.

So thank you very much.

DR. YANG: Thank you very much.

We are now at a hiatus within the Open Public Hearing portion of the agenda.

Panel members, again I'll remind you, please do not discuss or contact anyone about the meeting topic during the break. This includes discussion amongst yourselves or with any members inside or outside of the audience. Panel members, for your lunch, please follow the direction of the security escort. Also, please take all personal belongings with you at this time. This room is secured by FDA staff during the lunch break. You will not be allowed back into the room until we reconvene. We will reconvene promptly at 1:50 p.m. We will now break for lunch.

(Whereupon, at 1:08 p.m., a lunch recess was taken.)

A F T E R N O O N S E S S I O N

(1:55 p.m.)

DR. YANG: If we could all take a seat, then we'll go ahead and get started.

So now we will proceed with the second portion of the Open Public Hearing on the agenda. Public attendees are given an opportunity to address the Panel, to present data, information, or views relevant to the meeting agenda.

There has been a request to speak by 17 concerned citizens that are present today. As your name is called, please approach either the podium or the microphone in the center aisle. If you have slides or video, please approach the podium in the front. Also, if you have issues with mobility, Ms. Williams, who was -- who is right there -- will help you get to the microphone and put it at the appropriate height for you.

So there necessitates a little bit of out-of-order, so our first speaker will be Aracelis Sanchez. And pardon me if I mispronounced your name.

Do we have Aracelis Sanchez here?

Okay. Very good, go ahead.

MS. SANCHEZ: Hi. My name is Aracelis Sanchez. I'm here today for the JRC program. I was a former student at the Judge Rotenberg Educational Center. I was on the electronic device treatment. And as you

see, I was a successful story. I was rejected by 35 programs all around the country: DYS, DMH facilities. I was in the state hospital. I got kicked out of every program. I went to JRC. I was there about two and a half years, and I had the treatment; it worked for me. You don't see cuts, bruises, nothing. Right? All right.

So I'm here today to let you people know that this program is the most successful program, and if it wasn't for JRC, I would not be standing here today in front of you people. So I want you to please take into consideration -- and if you would like, go check out the program for your own eyes. Don't listen to all the garbage and rumors that you hear, because I am all for the Judge Rotenberg Center and the treatment. Because like I said, I would not be standing here today in front of you people. I either would be dead or in jail for the rest of my life.

I am now living on my own, have two beautiful children, and happily married. I drive. I'm in the medical field. I am a nursing assistant. And I have become very successful because of the Judge Rotenberg. So please remember that if it wasn't for JRC, a lot of people would be in a lot of pain and hurt out there.

I went into JRC tied down in a stretcher coming from a behavioral hospital from Virginia because I was rejected and kicked out of there after eight months. Unsuccessful. On 14 different psychiatric medications. Nothing worked. I was a zombie, a walking zombie. JRC

believed that off medications was the best thing for me. And you're damn right it was. Why? Because today I stand here in front of you as a grown person, successful, and that's what I want you people to see. JRC is a life rescue program for people that are severely in need, where they've been rejected from so many other facilities because they can't handle them.

DR. YANG: Excuse me, please. Wrap up.

MS. SANCHEZ: And they gave us the chance for a new life in a whole different direction. I have worked when I was at JRC, and I continue to succeed because of JRC. So, please, take it into consideration.

Again, it's Aracelis Sanchez, former student of JRC. And I thank you for listening.

DR. YANG: Thank you very much.

Next we have -- please. Brian Avery. Please approach the microphone.

MR. AVERY: Good afternoon. Prior to entering JRC, I exhibited serious self-injurious behaviors as well as aggressive behaviors while at home as well as in school. Such behaviors included head banging, hitting myself, running into the parking lot while at school as well as running into the street, stabbing myself with a pencil. Aggressive behaviors included hitting my parents, siblings, teachers; throwing objects at others; threatening others with weapons. Other behaviors included being disruptive during class, being noncompliant, disrespecting or disobeying my parents or authority figures. I

was also on a large amount of psychotropic medicine.

For the first year and a half I attended JRC, those behaviors continued and intensified in frequency. In spite of JRC using an extensive reward regimen, I spent much of my time needing to be restrained and made little academic progress. After a year and a half, I was placed on GED treatment. Over a four-year span, I received a total of 13 shocks, totaling 26 seconds of mild pain, which has enabled me to come off of my medication, improve my grades, integrate into the community, hold an in-school job, and ultimately transition back into public school, where I graduated close to on time. Since leaving JRC, I have held jobs in the community, have done extensive volunteer work, and currently live on my own.

Thank you.

DR. YANG: Thank you.

Next is James Butler.

MR. BUTLER: Thank you for holding this meeting. I am the former vice president of the Autism National Committee, founded in 1990, to work against aversives and for human rights. My own background is a master's in chemistry from Harvard and that I supervised pharmaceutical research for several years. My son is autistic, and I spend a lot of time as his caretaker.

The FDA should ban aversive conditioning devices that use electric shock because of the unreasonable risk of illness and injury. Electric

shock and aversives are inhumane. No one should be subject to pain and suffering in the name of treatment. Debate about whether people with disabilities can feel pain or need to be taught with pain belongs in the Dark Ages. The Department of Education, moreover, has said that interventions must be consistent with dignity and freedom from abuse.

These devices are unreasonably harmful. Their side effects, as we heard in the morning, are extensive. They cause pain. Students have developed psychological trauma and ill effects. In 2007, two students, who were shocked repeatedly in a hoax, experienced illness and injury. One complained about difficulty breathing after the 8th administration, asked for water after the 10th, and began to shake at the 13th. During a 2012 trial, videos showed the repeated shocking of another student, including his screams. An expert testified that he was in a catatonic state, subsequently.

There is no peer-reviewed research supporting electric shock or regarding the effectiveness and safety of the GED. What little there is, is sparse and outdated and does not meet modern research standards. I will add, at this point, that I've seen what it takes to get a drug from discovery through development into market, and if the GED were a drug, it wouldn't even be at the beginning of this process. Furthermore, it causes harm. It has no place. Twenty-first century decisions demand high-quality research. Many years of such research have shown that positive behavioral supports effectively modify challenging behavior without dangerous pain and other

side effects.

On the question of labeling, improved labeling will not eliminate the risk of injury from shock. Labeling cannot eliminate the pain and mistreatment of people with disabilities. Difficulty following instructions has indicated that it just won't work. The New York State report documented administration of shocks for minor infractions like failing to be neat or slouching in a chair. They also reported that students showered with the devices. During the 2007 hoax, the staff badly miscounted the number of shocks administered. Please ban these devices.

Thank you very much.

DR. YANG: Thank you.

Cheryl McCollins, please.

MS. McCOLLINS: My son is a former student of Judge Rotenberg Center. He was tortured on October 25th of 2002. As a result, he suffered from burns, fear, pain, catatonia, PTSD, and DVT. Deep vein thrombosis in his left leg was caused by the catatonia. The catatonia was caused by the shock. And I have medical evidence to prove it.

His torture all began because he refused to take off his coat. So you see, ladies and gentlemen, this is not about therapy. This is about control, abuse, and torture. The staff was exhibiting more behaviors than anyone in the room. The staff actually was out of order and out of control. Whoever is in agreement with this torture has antisocial behavior, and I'm

sure you all heard of Jim Jones, Charles Manson, Adolph Hitler. And two of them ran cults. And that's what JRC is. It's a cult. Run by sadists. But our disabled children are not masochists.

In 2012, I sued JRC for torturing my son. Their own expert witnesses never mentioned or never believed and never spoke and never said, during the trial, that this behavior was appropriate, effective, or that it worked. They had someone come in from Canada who was supposed to testify. We waited for a long time for him to testify, and I guess they flew him out because he decided not to.

I'm going to read you this: "JRC denies that Andre McCollins was injured by JRC or its staff and further asserts that JRC's behavioral treatment program for Andre was appropriate and effective." This was written by Michael Flammia and signed by him. So he is the only one that believed that my son's torture was appropriate and effective.

In addition, I never heard of GED-4s. That was introduced to me at the trial. I asked my attorney what is a GED-4? He says what your son was shocked with. I said I never heard of it nor did I ever sign up for it. There was a big emphasis on cameras. It was the reason why I chose the Judge Rotenberg Center, because I thought he'd be safe.

DR. YANG: Excuse me. Please wrap up.

MS. McCOLLINS: But what I found out was the cameras were there to make sure that the staff was shocking the children. Burns, pain, fear,

catatonia. My son is on lifelong Coumadin. He has to take Coumadin for the rest of his life.

DR. YANG: I'm sorry, I must ask you to stop.

We are changing the order slightly to allow for those with presentations to be grouped. So Diane Engster, please. Next.

MS. ENGSTER: Good afternoon. My name is Diane Engster. I received my law degree in 1984. I have been helping kids and adults with disabling conditions since I worked for the Massachusetts Office for Children in 1978. That long ago, this agency was investigating the unacceptable use of aversive interventions at the JRC.

Here is a story of a teenage girl who revealed her story in the *New York Times* in 2011. The young woman was admitted to the Institute for Living in 1961 and immediately was banished to the seclusion room. According to the *New York Times*, the girl attacked herself habitually, burning her wrists with cigarettes, slashing her arms, her legs, her midsection, using any sharp object she could get her hands on, and banged her head against the wall and later on the floor, hard. She prayed, I'm out of control, somebody help me, where are you, God?

They dosed her with antipsychotic powerful drugs and strapped her down for electroshock, which is ECT, 14 times the first session and then 16 times, but it didn't work. And then back to seclusion. She stayed there for 26 months and was considered one of the most disturbed patients. Her

medical treatment only makes things worse. But this remarkable person was able to discern that effective treatment must be based on facts: which precise emotion led to which thought, and which emotion led to the last gruesome act.

Years later, I find myself sitting in a large hotel conference room listening to an expert tell other professionals about evidence-based therapy that this lecturer had developed, known as Dialectical Behavioral Therapy. It's a nonviolent therapeutic treatment for emotional regulation of self-harm. I was also there looking for answers for intense urges for self-harm and suicide, like that young woman, but for me.

The lecturer was Dr. Marsha Linehan, who is considered to be a worldwide expert on DBT. Two key elements of her therapy have helped me: mindfulness meditation and validation, which I practice. And validation is the total antithesis to aversion therapy and administrating electric shocks.

DR. YANG: Excuse me. Please wrap up.

MS. ENGSTER: Okay.

Validation is very important. It's the recognition and acceptance of another person's internal experience as being valid. As I said, it was developed by Dr. Linehan. Dr. Linehan --

DR. YANG: Excuse me. Please stop. I'm sorry, but you'll have to sit -- thank you.

Next, Ian Cook.

MS. COOK: Hello. I am Ian Cook. My legal name is Hilary Cook. And thank you for having me here today.

I was a student at JRC from 2006 to 2009 and was on the GED-4 for the majority of the time I was there. The only good thing that the JRC did for me was taking me off of my medication. It turned out they were at the root of my problems. The GED, however, didn't help me at all, on the contrary. I had been put on the GED due to my previous aggressive behavior. That said, I cannot remember a single time I was ever shocked for said behavior.

Most of my shocks were for noncompliance or disruption. In fact, I was also subject to a method known as BRLs. While I was sitting in a restraint chair, a staff would burst into my conference room -- I was one-on-one alone with staff -- and screamed at me to hurt him holding a knife. Even though I did absolutely nothing and sat there in shock, not having any idea what was going on, I would receive a shock from the GED device. This happened a couple of times a week, at first, and left me in a constant state of fear, never knowing when I'd be hurt for no reason.

My experiences from the GED have affected me to this very day. I now suffer from a fear of authority, a fear of being controlled, and I panic when presented with either.

A side note. I was in an abusive relationship two years ago, and part of why I fell prey to it -- my belief -- is that JRC instilled a lesson in me

that it is okay for people to hurt me so long as they are trying to correct me.

I have, to the best of my knowledge, not experienced any beneficial effects, both either short term or long term, from the effects of the GED. I would strongly suggest, based on my personal experience and my ongoing difficulties, that the FDA ban the current and future use of the device.

Thank you very much for having me.

DR. YANG: Thank you.

Lauren Emmick, please approach the microphone or podium.

MS. EMMICK: My name is Lauren Emmick.

My daughter, Lian, has been receiving this life-changing treatment with the aversive conditioning devices for the past five years. My husband and I adopted Lian from China. She has a long history of extremely aggressive behavior. She has been through two day school programs and four residential school programs requiring at least one-to-one staffing. Because Lian was so aggressive, she was isolated from her peers in an effort to keep everyone safe. Consequently, she received little education and was rarely able to go out into the community.

Lian spent many long hours in timeout rooms with durations for as long as 19 hours a day. She also experienced years of physical restraints. During the six months prior to receiving the aversive conditioning devices, Lian had 159 restraints with a duration averaging 26 minutes. Eleven

percent of those restraints caused injuries to her or to staff members. Both of Lian's knees were severely injured due to restraints. Knee surgery was not an option because she wasn't safe.

By the age of 17 years old, she had been on 25 different psychotropic medications. Lian experienced many side effects, including over-sedation, drooling, depression, confusion, weight gain, headaches, and permanent hand tremors. Also by the age of 17, Lian had been hospitalized six times with an average stay of 31 days. She was hospitalized because she was a danger to herself or others. Starting at the age of three, we worked with a variety of psychologists, psychiatrists, behaviorists, as well as years of sensory integration therapy with occupational therapists.

Lian started with aversive conditioning devices at age 17. As a result, she is happier than I've ever seen her. She lives in a home with peers and, in fact, has two roommates. Lian has a job working in the school kitchen two to three times a week and continues working on academics in the school classroom setting. She is able to go into the community on field trips, goes out to lunch with me every week, and comes home monthly. She has had surgery on both of her knees and is now able to walk without braces. She is not on any medication and no longer requires restraint. She has not experienced any injury or illness as a result of the aversive conditioning devices.

What I find most surprising is that my daughter is thankful for

her program that includes these devices. She asked me why she didn't start this treatment when she was 10 years old. She tells me all the time that she's not ready to have the devices removed. She would likely react very negatively if you told her that the treatment was no longer available. I'm quite confident that restraints and injuries would return.

DR. YANG: Please wrap up.

MS. EMMICK: The aversive conditioning devices have allowed Lian to live a fuller and safer life. It is the only method that has worked for her. We are thrilled with her progress and pray that it will continue.

Thank you.

DR. YANG: Thank you.

Marcos Pucha.

MR. PUCHA: Good afternoon. My name is Marcos Pucha. I am from Brooklyn, New York. I attended JRC from November 2003 to June 2008.

Prior to attending JRC, I was a very aggressive, emotionally disturbed youth. I grew up in a foster care system. I was placed in group homes, and I was constantly in and out of psychiatric hospitals. I was slowly building a criminal record by getting in trouble with the law and being placed in juvenile detention centers.

I was put on many different psychotropic medications, which didn't help me function and made me sleep half the day. I was expelled from many schools due to constant fights with other peers. At 16, I decided to

become a dropout. At the rate that I was going, my life was heading in two directions, either death or prison. My foster mother had not lost hope in me, and after researching places, she knew that JRC was my last chance to change my life around.

When arriving at JRC, it was a whole new setting for me. In the beginning, it was a little hard to adapt. I was very aggressive and assaulted staff. They slowly started decreasing my medication and started using positive reinforcements. My aggressive behavior still continued. My mom decided to give the GED a try. When I was placed on the GED, I hardly didn't get that many. The most, I'd say, is eight throughout a two-year period. They were in no way harming me. They never scarred or burned me.

My aggressive behavior started decreasing rapidly. I was off medications, I could function better, and I was getting an education. I took advantage of the good opportunities JRC had to offer. After great progress, I was completely faded off the GED. I earned school independence, and I have a job as well at JRC. I graduated JRC in 2008 with a New York State high school Regents diploma.

I went back home and became a positive, productive individual. I was a youth advocate for troubled youth in New York City and assistant cook for Norwegian Cruise Lines. I've been happily married for five years. Me and my wife have three beautiful children. We try and do fun things with the kids on our time off. I am currently employed with JRC as staff. I'm an assistant

chef in the kitchen. I recently received my national certificate for food manager's license. I plan on starting my own food truck business in the future.

I am a firm believer of the aversive treatment because I'm living proof that GEDs do work. I thank JRC and its staff for getting me in the right direction. And without JRC and the GED treatment, I don't know how I would be today.

Thank you.

DR. YANG: Thank you.

Ilana Slaff-Galatan.

DR. SLAFF-GALATAN: Hi. I'm Dr. Ilana Slaff-Galatan. I'm a psychiatrist, and I completed my fellowship in autism research at the New York and Seaver Autism Center at Mount Sinai Hospital in New York.

I have identical twin brothers and a daughter with autism. My brother Matthew -- and I'm happy to pass this around -- banged his head and he had an over-five-month hospital stay. He had to have surgery to close his head, and he had to have intravenous antibiotics. He also has a history of scratching, biting, and picking his skin. The medications did not stop his behavior. In fact, he developed the deadly condition of neuroleptic malignant syndrome. He also has permanent tardive dyskinesia. He would throw his helmet at someone, and he was physically restrained. JRC was the only school that would accept him in the United States, as is the case today with

some of my patients.

The intensive positive behavioral interventions were not sufficiently effective. Reduction is not enough for this behavior. We need elimination. And the research shows that positive behavioral interventions do not necessarily give you elimination. The standard is a 90% suppression. This needs 100%. And even that 90% suppression is only in 50% of subjects, and if you do a good functional experimental analysis, it's two-thirds.

With the skin shock, the GED-4, he has not banged his head in over 20 years. He has had no side effects. The first year, he had to have 200 applications. He hasn't had any now in two years. He's happy, and he says he wants to stay at JRC forever, and he even asks to wear the device. When it was removed in February of 2011, for the first time in over 20 years, he had to go to the hospital for his self-injury. He broke both his eardrums.

Some people with autism, including his identical twin, developed seizures from psychotropic medication. And people with autism, even if they don't have clinical seizures, they could be at a higher risk for seizures, and antipsychotics and some antidepressants will increase that risk. Also, when you can't communicate your side effect, it gets very advanced and much more dangerous. People have died from adverse events from psychotropic medications, including in my own practice.

Just as the New York State Education Department does not approve the use of aversives, they also do not approve the one-to-one ABA

schools, despite substantial research evidence -- and also other states do approve them. So for my daughter, I'm paying $102,000 this year in school tuition --

DR. YANG: Excuse me. Please wrap up.

DR. SLAFF-GALATAN: Okay. And every year I have to file an impartial for reimbursement. I have tried GED. I won't try Thorazine or other psychotropic medications that have a remote, but possibly can kill me. Two people have been taken off GED. They came back to New York and died from their behavior. I don't want my brother --

DR. YANG: Thank you. Please stop and have a seat. Thank you.

Roger and Sharon Wood.

MS. WOOD: There is a small population of disabled children, including our son, Joshua, who cannot be treated effectively with the use of positive behavioral procedures alone and must -- and requires supplementation with the use of aversive therapies. And this is a little bit about Joshua and how we came to this conclusion.

Our son, Joshua, is profoundly autistic and nonverbal. He was diagnosed early by Dr. Geraldine Dawson, an autism specialist at the University of Washington. He received early intervention, ABA, sensory integration, everything you can think of, before he was two years old. When he became school age, at the advice of Dr. Ed Fenske from PCDI Child

Development Institute, we moved him to Virginia, into a day school at the Virginia Institute of Autism.

When he was young, he was manageable even with his self-injurious, aggressive tendencies. But because he was small, he was manageable. And when he attended VIA -- and he did okay, except on the onset of puberty, and that's when prescription medications began being prescribed. And his behaviors increased, and he was larger and more violent. The medications did not help. In fact, they made him worse. Psychiatrists prescribed many, and Josh would only scream after he took them and hold his head and then cry in rage. He was not psychotic; he was autistic. The drugs were not effective.

Joshua eventually attended a residential school in Maryland, Benedictine, which is very well known for their positive behavior analysis techniques and sensory integration. See, we tried everything for Joshua. When he was 15, he would cry, and his behaviors would escalate to the point where he would attack himself and others in the school, violently. He was very strong and unpredictable and could not control these behaviors.

It was mutually decided that this was not working for Josh, so the school sent him home on suspension, and before we could get him home, he aggressed in our car, almost causing an accident and requiring an ambulance and police vehicles meeting us and restraining us to get him to calm his violent rage. This is with our young daughter in the car. We could

barely keep him still. Three police officers tackled him to the floor and helped him as he cried and screamed in fear until an ambulance strapped him down and took him to the hospital. Sedation was ineffective in the hospital. In the middle of the night, he was escorted to a facility by ambulance, a temporary facility in Virginia, before entering the Judge Rotenberg Center by Angel Flight.

He was in a concrete room in this facility in Virginia, with a bed, beating his head, crying, taking ineffective drugs, strapped to his bed. He was filthy. He wet himself all the time. He was terribly depressed. At these other institutions, he had cracked his head open and he was bleeding. He wouldn't stop beating his head or his chin or aggressing.

DR. YANG: Excuse me. Please wrap up.

MS. WOOD: Okay. Anyways, before this, he was covered in bruises constantly and completely. He was bleeding from open wounds, self-inflicted, and out of frustration he could not control himself. So it was a living hell for Josh and our family. JRC is a godsend. It saved Josh's life. He's been there for five years. He's smiling. He's no longer restrained. He's taking no medication, dressing himself --

DR. YANG: I'm sorry. Please stop.

MS. WOOD: -- flying home --

DR. YANG: No, I'm sorry. Thank you.

Louisa Goldberg. Louisa Goldberg?

MS. GOLDBERG: I'm not sure why I'm on this session. I spoke before with BRI Parents and Friends.

DR. YANG: All right. Thank you.

Michael Cameron.

DR. CAMERON: I'm Dr. Michael Cameron, and I'm here in favor of the Judge Rotenberg Center. I'm a board certified behavior analyst. I'm also trained as an experimental psychologist and an expert in the field of behavior analysis. Within my capacity as a behavior analyst, I've worked in the field for over 25 years and in various formats, one as an applied clinician and a second as the chair of the Department of Behavior Analysis at Simmons College, which is an ABAI-accredited program. And I've published peer-reviewed articles on both positive behavior support and also regarding punishment technologies.

By way of full disclosure, I am an expert witness. I am paid for my time here and travel, and I have no financial stake in the Judge Rotenberg Center, nor will I benefit from the outcome of this meeting.

But I also stand here in front of you at risk, at extreme risk. There's not a line of people behind me from the behavior analytic community that's willing to do this. I may very well go back to my university and be dismissed as a result of what I'm about to say today. And I'm willing to take that risk because I believe, truly, in what is being done at the Judge Rotenberg Center.

As a result of my travels, I crisscross this country and do consultation, and I spend time in private schools, in public schools, and state hospitals and private hospitals, and home-based settings and school-based settings. And what I see uniformly over and over and over again is a sequelae of ineffective treatment, individuals who are subjected to polypharmacological treatment that is pain inducing and destructive to internal organs. I see individuals subjected to the use of physical restraint and mechanical restraint. These are people nobody wants to talk about. These are individual lives that are sequestered and pushed away and are not looked at by the community.

Over the last three months, I have visited the Judge Rotenberg Center and went in with a very critical eye, and what I found uniformly was some of the best behavior analytic treatment I have seen: individuals using functional behavior assessment, functional analysis, and using antecedent control strategies, reinforcement-based strategies. All of those strategies you saw on the screen earlier today are being used there.

One of the things I would like to emphasize is that their emphasis is not on shock. Their emphasis is on the entire protocol and a package used to develop skills and abilities so that the individuals will not be subjected to shock.

DR. YANG: Excuse me. Please wrap up.

DR. CAMERON: I've seen the outcomes and trends of health

outcomes, educational engagement, family reintegration, community reintegration, and educational advances. I ask you in the spirit of the right to effective treatment. For some individuals, I believe that primary salient punishment is what's necessary in order to compete with their repertoires.

Thank you.

DR. YANG: Excuse me. Thank you.

Arthur-Michele Perazzo.

MS. PERAZZO: Good afternoon. I am Michele Perazzo, and this is my husband, Arthur Perazzo. Thank you for giving us this opportunity to share with you how the GED skin shock treatment has transformed our son's life.

Our son, Michael, is 28 years old and has been at JRC for 11½ years. He is diagnosed with autism spectrum disorder without intellectual impairment and has severe obsessive-compulsive behaviors.

I am a retired New York City social worker, and my husband is a retired New York City schoolteacher. Both of us have worked with children with challenging behaviors, and yet we were not prepared for those our son exhibited.

We used our education and experience to obtain the best help available for Michael over the years. That help included seeing several prominent psychiatrists who prescribed many different medications which were not only ineffective, but had serious side effects. Michael also had

behavioral programs and counseling and a specialized day school. The end result was that at age 14, he no longer was going to school and was housebound. If we tried to interfere with his compulsions or set limits, he became aggressive.

Michael stayed at his first out-of-state placement for almost two years, but they ended up dumping him in a psychiatric hospital when they could no longer handle him. The clinical director said that if it were her child and the next placement didn't work, which it didn't, she would find a place that put few demands on him and make him comfortable. That was warehousing, and we would not give up on our son.

The second out-of-state locked-door placement lasted about a year. They called us in the middle of the night to say that they didn't know where he was. He ran away while on a walk with staff, and the police were called to find him. He made no progress there and had takedowns and isolation and timeout rooms for long periods of time.

What do we do at this point? We were desperate, but not ignorant, as some would say. Our research took us to JRC and the GED device. We tried it ourselves. And though it certainly got our attention for a couple of seconds, we didn't know if it would work for our son. Michael has a high tolerance for pain.

MR. PERAZZO: JRC was more than willing to accept a child who was tossed out of one school, failed at another, and had refused to go to

school or wear glasses. We specifically sent Michael to JRC for the GED since we had exhausted all other treatments. After a positive-only reward program, a period of five months, and with court approval, Mike was placed on the electronic device. Although he said it doesn't hurt that much, it did work. We were finally able to take him out for meals, to the movies, and finally to visit home. Why did it work for him? Michael not only didn't mind restraints and timeout, he may even enjoy them.

DR. YANG: Excuse me, please wrap up.

MR. PERAZZO: The GED application did not provide secondary gains. Sadly, there is a small percentage of the disabled population that medication and positive-only reward programs does not work on. We are beseeching you not to take this away from him. Look what it did for Michael. Michael is now coming back to New York --

DR. YANG: I'm sorry, please stop.

MS. PERAZZO: And going to college.

DR. YANG: Thank you.

Gregory Miller. You have three minutes.

MR. MILLER: My name is Gregory Miller. I used the GED-3 and the GED-4 -- GED-3A and GED-4 devices on my students at the Judge Rotenberg Center, where I worked for over three years as a teacher's assistant. I believe that JRC has misled you today when answering your questions, and I could tell you and show you the truth if you gave me time. I

gave JRC a two-week notice prior to my resignation, and I wrote two letters to JRC's executive director, in which I stated my opposition to the GEDs. I have those two letters today to counter JRC's misinformation about me.

My first priority is to tell you that I would never have used the GED-3 instruments had JRC told me and others in training that the GEDs had not been approved by the FDA, as JRC falsely advertised even on their website until 2012. In the screen, you'll see that I've got some color photographs. I can only flip through those injuries obtained from the DPPC, Massachusetts Disabled Persons Protection Commission.

Something is wrong with the photographs up there. The machine is not working. They're like wiped out. So anyhow, you can see your printouts of these injuries. They are very real.

Please picture yourself in -- are any of these working? This thing is not working. Please picture yourself in a classroom of 12 to 14 lower-functioning, nonverbal students. Students begin to whimper and then crying and showing extreme anxiety that I cannot put into words. A staffer reaches for a pencil in his pocket near where the GED sleds are hanging from his belt. I was required numerous times, along with other staff, to shock 6 or 7 students simultaneously, out of 12 students in the room, when some staff would merely reach for a pencil or reach for a student's recording sheet or pick up a GED sled to take a student to the bathroom. They think the GED is for them and exhibit behaviors in an uncontrollable panic, even though they

know they will get shocked for those behaviors.

The following are images of behaviors that I captured directly off of Andre McCollins' recording sheets the day we see him shocked that concretely demonstrate the typical and most common types of anxiety caused behaviors for which the lower-functioning students were frequently shocked.

Okay. Some of these are missing here. Please do follow on your sheets.

Pulling on their electrodes, trying to pull them off of their arms. The shock is for any attempt to remove devices. Throwing down their task on the table. And they have to shock them for throwing objects. Grabbing the hand of the staffer, just reaching near the activation box, because most students grab them. So most have "grab" on there. But if they grab the hand, not even trying to be aggressive, just hold your hand away from the device, you have to shock them for a grab, if they have it, or for any physical aggression towards others, including attempts.

Again, this is right off of Andre's recording sheets as examples. They can't deny that they're not shocking kids for this. This is right off of government -- from the DPPC. Dropping under the table, like we can see Andre do in the videos, dropping under the table, throwing themselves on the floor.

DR. YANG: I'm sorry, but your time is up. Since the slides

aren't working, do you have a video clip that you want to show for 10 seconds?

MR. MILLER: I just wanted to finish this thing. Oh, no, I'm not going to be able to show a video.

DR. YANG: Okay. Well, I'm sorry, your time is up.

LCDR RUSSELL: We can allow you for the clip of your video, since our projector is not projecting your pictures.

MR. MILLER: Oh, were you able to upload the mp4?

LCDR RUSSELL: Yes.

MR. MILLER: Okay.

LCDR RUSSELL: So we will allow you --

(Video played.)

MR. MILLER: So just briefly, she's having extreme anxiety. Your computer is not working. But it's extreme anxiety. Imagine a whole slew of students grabbing for this, this kind of thing, and we have to shock them for the behaviors that they have.

DR. YANG: I apologize for our AV, but thank you.

Next is Jennifer Msumba.

(Video testimony.)

MS. MSUMBA: Hi. My name is Jennifer Msumba, and I wanted to make this video as my opportunity to express what happened to me when I was at the Judge Rotenberg Center, in regards to the GEDs and how it

affected me.

I was there from the year 2002 -- March 2002 until April in 2009. When I would get a GED, I would get -- most of the times I would get a very bad muscle cramp that would last me for one to two days. I would get burn marks on my skin. They like to call them small, raised bumps. They're burn marks. It's electricity going into your skin, and it's very itchy and it stings afterwards, and you have these circular marks where you got the GED.

I also at one time was given several GEDs in one leg in a row, and I had a terrible pain shoot all the way through to my foot. And after that, I had no sensation in my skin on the lower half of my left leg. And for about a year, if I would touch my skin, I couldn't even feel anything that touched my skin, from that.

Also the GEDs will, what they call, misfire a lot. That happened to me in double digits, where it would go off by itself maybe if it got wet. One time I got caught in the rain. Other times, if they give a GED to someone else nearby and that device is too similar to yours, it can set yours off. Then I had times when the staff made mistakes and mixed up whose device they're using. So they're meaning to give a GED to another student, and they give it to you. I've seen some people's just go off and keep going off and going off over and over, and staff would literally to have rip open the bag and pull out all the wires to get it to stop. These are things that you were getting shocked for no reason at all, not even for behavior. It's an accident, and it happens all

the time.

It's not safe. It doesn't feel safe. I ended up having nightmares weekly, if not nightly -- at least once a week -- about JRC and the GEDs, about being on the GEDs. In these nightmares I'm getting shocked. During the day, if I hear certain noises, like the Velcro they use to keep them closed, I freeze. I feel like it's about to happen to me. Or if I'm having a hard time, I start to think I'm there again and that I'm going to get shocked for it.

I've been to dozens of horrible places, hospitals, residential schools --

DR. YANG: That was three minutes. Can you stop the video?

MS. MSUMBA: -- and I have never once had a nightmare about any of them.

(Video stopped.)

DR. YANG: Thank you.

Shain Neumeier.

MS. NEUMEIER: Hello. My name is Shain Neumeier. I'm an autistic person, and technology permitting, I will be showing you an example of how shock is used; that in its defense, JRC's only defense was that this, the treatment plan, was followed. This is what the GED use looks like when it's being used as it's supposed to be used on the weaker of the two devices presently used at the JRC.

I should warn anybody, first of all, who has PTSD, that they may

be triggered by this footage, watching somebody being restrained and shocked. And if anybody has epilepsy, the flickering may trigger a seizure. Just to warn anybody.

(Video played.)

MS. NEUMEIER: If that is what shock is supposed to look like, if that's what aversives are supposed to look like, there is no question that the harms far outweigh the benefits, both for any prospective use and for the 71 people still being subjected to the same kind of shocks -- or more severe -- that Andre McCollins faced on that day.

Thank you very much.

DR. YANG: Thank you.

Vito Alvenese. Since you registered after the deadline, you get one minute.

MR. ALVENESE: Yes. Thank you for having me testify one minute. I am Vito Alvenese, and I come from Brooklyn, New York.

I have a son that has a traumatic brain injury. He's been in a couple of residential treatment programs, was abused and neglected. While he didn't go to the Judge Rotenberg Center, I've been involved for 25 years with the center, with other advocates, to try and shut this school down. What they are doing to these children is torture. The United Nations has written to the Obama Administration and said to look into this matter, as it is torture to these children.

And I don't have that much more to say, but I'm asking the FDA to take a serious and deliberate action today and banning the use of this torturous thing.

Thank you very much.

DR. YANG: Thank you.

MR. ALVENESE: Oh, one more, if I've got some time.

In 2005, I had a law passed in New York, signed by Governor Pataki, called Billy's Law. The intent of that law was to repatriate all children from out of state --

DR. YANG: I'm sorry, please wrap up.

MR. ALVENESE: -- all out-of-state --

DR. YANG: I'm sorry. Thank you. Please take a seat. Thank you.

This morning, from the organization Open Public Hearing session, there was one organization that registered, but misregistered, so we are going to allow them the four minutes.

Occupy JRC, if you're here, could you please come to the podium?

MS. MINTON: Thank you. Sorry about this morning's mix-up.

You know, one of the first tenets of treatment and care -- the Hippocratic oath: First, do no harm. These shocks do a lot of harm, and they may appear to be helpful and that people stop doing the behaviors that they

have been targeted for, because of the shocks. But the reason they stop doing it is not because the underlying emotional trauma is being addressed or the underlying condition is being addressed; they stop out of fear. They're being trained to be compliant.

You know, if you get a skin shock every time you say ice cream, you're going to stop saying ice cream pretty quick, I would bet. And when you're giving people treatment, you want to work with them, not against them. Punitive treatment is not -- it just teaches people to behave out of compliance, and that's not what you want to do.

You know, when I met with my -- when I meet people and I tell them about the Judge Rotenberg Center, the first thing they say is often, how is this legal? And the other thing I hear when I talk to other people is, if they're getting this treatment, they must really need this treatment. That must be the only thing that works.

You know, I'm autistic myself, and it could've been me, it could be any of my friends. I know some nonspeaking autistic people that have told me their behaviors are because they're frustrated. They can't communicate in any other way. All behavior is communication, and they're trying to communicate, and the only way they know how -- and sometimes the behaviors that are targeted are the only way they know how to communicate and say no and they just -- I'm sorry, it's just emotionally hard to talk about this. But they get shocked and it's no way -- it's not humane, and the fact

that some people are so blasé about the fact that it's done to disabled people, as the lady from ACLU said, and only disabled people, it really goes to how we as a society think about disabled people as not deserving of the same rights and protections as other people and thinking that this is the right way to go in terms of treatment. And it's not.

You can get a lot farther, I think, by showing compassion and just sitting with someone and saying, you know, why are you acting this way? Or just showing the willingness to listen. And I think that that's a much better way to approach people in general, any human being. You know, you don't have to shock them to get them to do what -- yeah.

Okay. Thank you very much.

DR. YANG: Thank you. And thank you to all of the speakers at the Open Public Hearing.

Does the Panel have any questions for any of the Open Public Hearing speakers that have presented today? If so, please indicate to me that you do, and keep your questions brief and concise.

Dr. Fost.

DR. FOST: Norm Fost.

I don't know who to direct it at. Almost anybody could answer. We've heard from many people today that this is not a problem, that is, that there are effective treatments that are positive and compassionate and so on, and that these aversive remedies aren't needed. We've heard from others

that they are needed, that there are many children and adults who fail conventional treatments.

So I guess I would ask someone from the first group, who says that this is not a problem, if you think that the second group is not telling us the truth or they just have had incompetent therapists and need to get to better places. Can there be any agreement on the factual question about whether there are a substantial number of children or adults who fail what we might call positive treatments that are ineffective?

DR. OLIVA: Dr. Christopher Oliva.

There is a lack from research to practice -- it's in all fields, I've heard -- 20 years. And we're just -- the use of the advanced technology, behavioral technology that we have, is very uneven in its use and application. And there are extremely effective procedures, antecedent approaches, uses of addressing precursor behaviors, prevention procedures that are not thought to be ethical by many behavioral clinicians. And what many of us have learned in the field is that we start by prevention, and we systematically teach adaptive skills of ways that individuals have their needs met appropriately. And we know how to do it with instruction and intervention and based on functions of behavior.

DR. YANG: Thank you.

DR. OLIVA: It is not universally embraced.

DR. YANG: Any other questions from the Panel?

DR. CAMERON: May I respond?

DR. YANG: Please approach.

DR. CAMERON: One of the things that I encourage the Panel to consider is that many of the publications regarding positive behavior support, if you look at the profile of that individual that that treatment methodology worked for, what you'll find is that if you match to the profile of an individual from the Judge Rotenberg Center, there is not a match. The people that I've seen at Judge Rotenberg Center, many are dually diagnosed, many have long histories of treatment-resistant behavior, many individuals are in their twenties and thirties, and much of the literature on positive behavior support is done with young children. I have a real concern, from a scientific standpoint, with respect to the external validity of those findings. I'm not finding that it can be applied uniformly across all individuals.

So I don't think that individuals are not telling the truth with respect to efficacy. I just firmly believe that there is a population that is treatment resistant, that does require something different that will compete with their maladaptive behavior.

Thank you.

DR. YANG: Thank you.

Let's move on. Dr. Connor and then Dr. Augustine.

DR. CONNOR: Jason Connor.

So this question is for a single person -- I don't care who it is,

but one person, from before lunch, from an advocacy group, I would like to approach. And my question, while whoever that is approaches, is -- you know, we talk about efficacy, but no efficacy is 100% and we keep going down, down, down the chain, and it seems like patients who get to the JRC are, sort of, this is a last resort. And we've heard from parents whose children went to very good and very effective in most cases, and I'm sure, very expensive centers where it didn't work and they were removed.

So I would ask one of the leaders of an advocacy organization, like, what would you say to the parents who are sort of begging that this continue? I would just be interested to hear that perspective. Like, you know, do they need to try more centers? Is it better to have a child who is largely sedated, with that quality of life versus, it sounds like sometimes, higher quality of life, but maybe living in fear, which is what some of the other patients who have been there would say?

MR. NE'EMAN: This is Ari Ne'eman from the Autistic Self Advocacy Network.

This is actually not a new dynamic, where there are very similar conversations around institutional closure, around supporting people from other restrictive settings into more integrated settings. You know, between 1960 until the present, almost 200 institutions for people with developmental disabilities were closed, and very frequently you did see parental opposition there, which largely dissipated after people were effectively supported in the

community.

It's been our experience, at least, that one of the driving forces behind that parental opposition is that at the time a parent places their child within a restrictive setting -- and I think we can all agree that the Judge Rotenberg Center and this aversive device is one of the most extreme forms of restrictive setting -- they are being told by a professional in their life that this is the only option for their child. And it is very difficult at an emotional level, having made that, I'm sure, heart-wrenching choice, to then realize later on that that was an error, to then realize that a decision that, by design, hurts their child was one that they did not have to make.

And so cognitively, that is something that parents have a very hard time realizing until after their child is supported into a more integrated setting. It's a very familiar story. We've seen it in countless examples around other restrictive settings. And I would point to the ample testimony around research and best practice as proof that people can be supported. It's just a matter of facilitating that transition and not allowing what families might have been told decades ago to hold the day today.

DR. YANG: Okay, thank you.

Let's move on to Dr. Augustine's question.

DR. AUGUSTINE: It seems that there is a range of experiences as it relates to pain from the shocks themselves, and I'd like to hear from either a former JRC patient or family member of a former JRC patient as it

relates -- who had a beneficial or who had a positive experience -- as to what the shocks felt like for them or what a parent saw as it relates to that.

MR. PUCHA: Your question is, like, what we felt when we got the shock?

DR. AUGUSTINE: Yes. So you had a positive experience. What did the shocks feel like for you?

MR. PUCHA: It's just a two-second shock, like -- it's like a bee sting basically, and it doesn't leave any marks on your skin.

DR. AUGUSTINE: And I think there's a parent or a set of parents sitting next to you. For your child, who I believe still is using the GED, what do you see when a shock is administered?

MR. WOOD: We did not take lightly our choice to put our son, Josh, in JRC. We visited twice. I had the application applied to me both times, and I've had it applied since. It's a shock to the skin. It tenses the muscles, and then it's gone. And that's what I felt with that.

And to address each person as an individual, I think we blanket what works for other people, other autistics. I think it's great that those programs are there. We went down that road. We followed ABA. We went to the best schools we could find. We hired therapists. And JRC transformed Josh's life. You talk about dehumanization. The Virginia Commonwealth Children's Center was a dehumanizing experience for us and for our son. JRC has been a godsend. And I think there's so much rhetoric about using these

words, "abuse" and "dehumanization." There are a lot of other programs out there that do that, as well, in institutions.

DR. YANG: Thank you.

Are there any other questions from the Panel?

Dr. Reppas.

DR. REPPAS: My question is for any person or family member who had -- who spoke in support of the JRC. And I guess my question is, I wonder the extent to which you can uncouple the experience of having been there from the use of the aversive stimulation, and is it possible that the good experiences came about because of the type of care that was delivered independently of the device that we're talking about today?

DR. SLAFF-GALATAN: My brother has been faded off the GED a number of times, and like I said, when he was, he had to go back to the hospital. But they do have -- he's on seven positive behavioral contracts at once. He has multiple contracts during the day as well as earning reinforcers from the contract store or earning -- looking at his maps or whatever. And he gets these -- he's on these contracts so many times and also he has the functional communication training, which I like, which unfortunately a lot of programs in New York don't do and don't do that intensive positive reinforcement. And yes, it's wonderful to see that, but I understand the need for the skin shock because, like I said, when he's gone off it, even despite all of those positive interventions, he's had to go back on it in the past.

DR. YANG: Thank you.

Since I see no other questions from the Panel, I now pronounce both sessions of the Open Public Hearing to be officially closed.

UNIDENTIFIED SPEAKER: Excuse me. Can I respond to the last question?

DR. YANG: No, I'm sorry, not at this point.

We will now proceed with today's agenda. We will now begin the Panel deliberations. Although this portion is open to public observers, public attendees may not participate except at the specific request of the Panel Chair. Additionally, we request that all persons who are asked to speak identify themselves each time they speak, to help the transcriptionist.

There are three additional questions for the FDA from this morning, and I will be calling on those first. But if there are any other questions for the FDA or the JRC, please keep this in mind and indicate to us that you have further questions.

Panel members, please keep in mind that time is of the essence. We want to ensure that we cover each topic area that has been addressed during this and the Panel questions.

So let's start with -- Dr. Peña would like to make a comment.

DR. PEÑA: Sure, thank you. I'd like to make a few statements for the Panel's considerations.

First, these procedures are intended for the Panel to make

recommendations in response to questions and not specifically will be asked to ban or not ban devices. The meeting is intended to provide valuable information and perspectives that will help inform FDA's deliberations.

The second point is that, based on our understanding of the current laws in Massachusetts, the Department of Developmental Services amended its behavior modification regulations in October of 2011 in order to ban all schools in Massachusetts, including JRC, from using certain aversive interventions unless a child had a court-approved treatment plan that allowed for their use prior to September 1st in 2011.

A third point is that issues about enforcement actions, inspections, and other related actions toward one or more manufacturers is not within the scope of the Panel's deliberations today.

Fourth, to clarify a question that was raised by the Panel about other information that we may be aware of, and in the context of JRC's comment about clinical data that was submitted for clearance for their devices, it was based on a comparison to pre-amendments devices, and clinical data contained case report forms, literature reviews, and references. None were prospective, and data was of the same quality of the data we have discussed earlier -- presented earlier this morning.

There's been some additional labeling questions. I'm going to turn to Dr. Bowsher to respond appropriately.

DR. BOWSHER: Yes. I believe somebody had asked to see a

copy of the user manual. We have copies going around to Panel members. I will put it on the screen, but I was wondering if that person had a specific issue -- question so that I could go to the proper location.

DR. YANG: That was Dr. Connor.

DR. CONNOR: No, I just wanted to see the label. So thank you.

DR. BOWSHER: That's good enough?

DR. CONNOR: Yeah. If I do, I'll let you know.

DR. BOWSHER: Okay, great.

DR. YANG: Let me remind you that anyone that's sitting on the front row that's not FDA, could you please move back to the back of the room?

So let's move on, then. Three Panel members had questions for the FDA that were left this morning. Let's start with Dr. Green.

Okay. Dr. Augustine.

DR. AUGUSTINE: I had a question for Dr. Park. As we consider multiple devices as a group, the GED-4 stands out a little bit to me as potentially being different, given the amount of current that can be delivered and substantially increases as compared to the other approved devices.

And so in review of the potential adverse effects or risks of these devices in the literature, is there a sense that there is a higher rate or that most of the risks that are reported seem to correlate with higher degrees of current? It sounds like, in older literature, really not much is reported as it

relates to adverse events, and most of the data presented are from more recent years. Are those in association with the use of the GED-4, or is that not so clear?

DR. PARK: Thank you for that question. This is Larry Park from FDA.

If you look at the literature review and the data that we do have, we actually did try to see whether we could identify any trends with regard to output and level or type of adverse event reported. And one thing is that the types of devices that were used in the literature review are all over the board. So some of them we had cleared at FDA, some of them we had not, and some of them were pre-amendments devices, I believe. And some of the studies actually came from outside the United States, so the FDA wouldn't have jurisdiction over those devices.

The other thing I would say to preface the conclusion is that, in addition to current, Dr. Bowsher put up a slide showing a whole bunch of other parameters, stimulation parameters, that might be related to perception of noxious stimuli and/or effectiveness.

So from our understanding, it's not just overall level of current that makes a difference, given that it's a very complicated situation. And even if it were just related to the amount of current used, looking through the data that are available, we weren't really able to identify any perceptible pattern of certain types of adverse events or severity of adverse events

related to different stimulation outputs.

DR. YANG: Okay, Dr. Connor. First of all, did you have another question? You were on the list from this morning.

DR. CONNOR: I think my question is for JRC, not for FDA.

DR. YANG: For JRC.

Okay, Dr. Miles, are you for --

DR. MILES: Yes, a follow-up question on that. Is JRC using 1, 2, 3, and 4? Or just 3? It's my understanding that they're just using 3 and 4, and it's my understanding that 3 and 4 were specifically created to increase the noxiousness level of the stimulus.

DR. BOWSHER: So I would let the company respond to what they're using. To our knowledge, they're using the 3A and the 4. And to the best of our knowledge, the 3A output is very similar to the cleared device, and the 4A is similar, except the output current is approximately three times higher. But I would let the company confirm that.

DR. YANG: Dr. Peña.

DR. PEÑA: I just would like to make sure that the Panel stays sort of at the level of devices as a general class, the general issue of aversive conditioning devices, and try not to delve into specific matters or interactions related to a particular manufacturer, if that could be upheld.

DR. YANG: So, Dr. Kim, is your question for the FDA or for JRC?

DR. KIM: FDA.

DR. YANG: Okay, please go ahead.

DR. KIM: This is a question for both Dr. Como and Dr. Park. The big issue is the quality of the scientific data for all types of treatments for serious self-injurious behavior and aggression. And having reviewed some of the papers you sent, I guess my question is -- for example, there was a review from 2002 that reviewed 396 papers, but that amounted to a total of 700 patients.

So my question is for the positive behavioral studies as well as for the ESD studies or punishment-based studies. Are they similar types of studies and similar types of quality of data, or is one group much better than the other?

DR. COMO: Sure. Thank you, Dr. Kim. Peter Como from FDA.

Unfortunately, the review of the literature sort of revealed two general themes. One, a lot of the literature is old, number one. Number two, they seem to not be prospective, controlled clinical trials like the standard we have today for any type of product. They tend to be single case reports or small case series. They are relatively uncontrolled. The outcome measures range from a clinician observing that the behavior seems to have decreased, to some quantitative assessment of reduction in behavior.

So I would have to say, overall, the quality of the studies, with the exception of a few of the pharmacologic studies in which they were randomized controlled studies, certainly don't meet the bar or the standard

that I think most scientists would accept today. But, again, a lot of these were published in the 1970s and '80s. So, overall, the evidence is about the same, be it a positive-based type of program that we talked about, or even some of the negative studies -- for example, using bitter substances or water mist spray or ammonia -- are also pretty much single case reports or small case series.

Did I answer your question?

DR. YANG: Thank you.

Mr. Mikita, is your question for the FDA or for JRC?

MR. MIKITA: FDA.

DR. YANG: Okay, please proceed.

MR. MIKITA: Okay, two questions. Can you state for this Panel succinctly what are the -- what was the last device that the FDA approved that the JRC was permitted to use?

And my second question is, could you clearly state what was the mistaken communication given by the Agency to the JRC, relative to a specific device and the exemption that was first given and then withdrawn?

DR. BOWSHER: I'll take your first question and then turn it to Mr. Amatrudo for your second.

The last device we cleared was a GED from the JRC.

MR. MIKITA: Okay, that covers a big umbrella. Okay, so is it GED-1?

DR. BOWSHER: It would be equivalent to the GED-1. Under the clearance we called it the GED. They also call it the GED-1, since they've developed three more models.

MR. MIKITA: What was the year?

DR. BOWSHER: That was 1994.

MR. MIKITA: Okay, thank you.

MR. AMATRUDO: Vince Amatrudo, Office of the Chief Counsel, FDA.

Again, issues pertaining to JRC's 510(k) violations and our erroneous communication to them, that they were exempt back in 2000, are not directly relevant to the issues before the Panel. As I explained earlier, we erroneously told them that they were exempt under a regulation providing an exemption for licensed practitioners. We determined they are not; they are a device manufacturer. But, again, we urge you to focus on the issues before the Panel and not compliance issues related to JRC.

Thank you.

DR. YANG: Thank you.

Dr. Stebbins, is yours for the FDA as well?

DR. STEBBINS: Yes, it is. This is for Dr. Peña, particularly for the second point that you were raising about the Massachusetts ruling of 2011.

Two questions -- a two-part question. Is that currently in

force? And, secondly, was it that the device was only to be used on existing cases, or the device was to be used on existing cases and cases that had a court order?

DR. PEÑA: So I'm going to turn the question over to you, Vincent Amatrudo.

MR. AMATRUDO: You're asking about the Massachusetts ban? I believe the ban applied prospectively, unless the child had a court-approved treatment plan prior to September 1st, 2011.

DR. STEBBINS: So that's my key question. They had to have the court-approved plan prior to that date. So they cannot do new cases; they can only use existing cases.

MR. AMATRUDO: Yes, I believe that's correct.

DR. YANG: Dr. Bickel.

DR. BICKEL: I was wondering if the FDA could advise us of whether there are -- which medications are approved for reduction of self-injury in developmentally disabled adolescent children and adults, and in the data that you reviewed for that indication, what was the efficacy that was reported?

DR. COMO: Sure. I have a backup slide on that for both risperidone and aripiprazole. So that's the official -- that's the labeling. As you can see, it's indicated for the treatment of irritability associated with autistic disorder, including symptoms of aggression towards others,

deliberate self-injuriousness, temper tantrums, and quickly changing moods. The efficacy was established in three short-term trials in children and adolescents ages 5 to 17. I certainly have all of those details, if you need them, in terms of the --

DR. BICKEL: So if there was a measure of clinical improvement, could you just give us what the percent of the sample that was improved in the active?

DR. COMO: Yes. So the first trial involved 101 individuals ages 15 to 16. They received twice daily doses of placebo and Risperdal, 0.5 mg to 3.5 mg per day. They used one of those scales that I had listed in my presentation, the ABC scale and a clinical global impression. I'm trying to see what were the actual results. So basically what they did is, is they looked at a significant change in the scores and found that there was a statistically significant drop in the placebo low- and high-dose groups, with the active drugs being statistically different from the placebo.

The studies did include a clinical global impression, but as I think most are aware, a statistically significant result does not always mean a clinically meaningful result, although the clinical global impression scale might capture that to some degree.

Do you want the information for aripiprazole?

DR. BICKEL: What I'm interested in is -- so that means that a larger number of individuals showed a reduction on those items. I'm asking,

did they report what proportion of individuals showed a positive response in the two groups versus which didn't respond?

DR. COMO: Yes, they really reported -- they didn't do a responder analysis, and mainly it was a mean reduction on the ABC irritability scale. And let me just correct that. Actually, the low-dose risperidone group and placebo did not differ statistically -- my apologies -- to correct that. They did look at long-term efficacy following an eight-week double blind. So 63 patients went into an open-label study, and they continued to maintain a somewhat positive response. But that was open label.

I can certainly talk about aripiprazole if you would like.

DR. YANG: Yes, please.

DR. COMO: Okay. So the labeling for aripiprazole is essentially the same. The efficacy was established in two eight-week trials in pediatric patients, with the irritability associated with autistic disorder again including symptoms of aggression towards others and deliberate self-injuriousness.

So, again, these studies used -- especially since aripiprazole came after risperidone. So you follow the same protocols to get approved. So they also used the aberrant behavior checklist and a clinical global impression. And basically, again, it was sort of basically the similar results. I think some of that information is in the Executive Summary. If not, I can certainly elaborate more, if you need.

DR. BICKEL: Well, on both of these, I'm very interested to find

out what proportions of people in the active group respond versus -- or didn't respond, right? Because that's very relevant to understanding whether there is adequate treatment and it was approved therapies.

DR. COMO: Right. From my reading of those trials, again, they did not conduct a responder analysis. So they were just looking at mean change scores on the ABC scale and the clinical global impression of change.

DR. BICKEL: What years were those?

DR. COMO: I believe risperidone was approved for this indication in 2006, and Abilify was in 2009.

DR. YANG: Dr. Peña, you had a comment?

DR. PEÑA: No, no comment right now.

DR. YANG: Are there any other Panel questions for the FDA?

Dr. Kim.

DR. KIM: Can I just follow up on the question about the two drugs? I was a little bit confused reading the review on your section, because on the one hand these two drugs are approved in double-blind, randomized controlled trials.

DR. COMO: Yes.

DR. KIM: But then it goes on to say that the studies are limited to very small case studies. Now, my interpretation of that was this -- and you can tell me if I'm wrong. These studies for the drugs were for general treatment of irritability symptoms for autism. So one of those, for example,

the aripiprazole, if I recall correctly, they did a retrospective analysis -- subscale analysis -- and found that the self-injury sub-score was actually quite low in those trials, and there was no statistically significant difference of the effect of aripiprazole, for example.

So I don't quite understand why -- I mean, you're going to have to sort of explain a little more. My understanding is that there isn't evidence for drugs treating serious self-injury. That was my interpretation. You can tell me if I'm wrong.

DR. COMO: Right. Well, first of all, your conclusions are correct. And I'm not trying to beg the question, but I can't really speak for our sister center, CDER, in terms of what the approved labeling was. That's what the label gave, recognizing that the main effects were mainly on irritability and less so on some of these other behaviors. But the labeling is what the labeling is, based on CDER's review of the data and their discussions in determining to approve these two drugs for an expanded indication. So I apologize, I'm not trying to beg the question, but we don't have a representative from CDER here to address that in more detail.

DR. PEÑA: Right. I think these types of questions are probably more appropriate to address to the Center for Drug staff. But if you're interested in, like, responder analysis or clinical trial design, we can certainly respond to those types of questions. But if there are specific questions about approval decisions for drugs, we should probably avoid that.

DR. KIM: My question wasn't about the approval process, but the overall evidence base. What I gathered when you made the statement in the review, that there wasn't a lot of systematic data for treatment of serious self-injury --

DR. COMO: Right.

DR. KIM: -- you were saying -- I could be wrong -- that these things were approved for a more general indication, and specific data for very serious injuries were a different matter. Now, is that right or wrong?

DR. COMO: I don't believe that the studies that were done to get the indication for autism distinguished between serious versus so-called non-serious self-injurious behavior. So yeah, I don't really know. I'm pretty sure that wasn't done. If you recall, in my presentation, too, when I talked about risperidone, I did emphasize that the data was stronger for irritability, with less effect on self-injurious behavior. We can call that slide back if you need to.

DR. YANG: If I might speak for myself and for the Panel, I don't believe that we are asking questions at all about the approval process in CDER. But given that we were given the Panel questions this morning and Question 1 gets at are there adequate other treatments, I think that's why Dr. Kim and Dr. Bickel --

DR. COMO: Sure.

DR. YANG: -- and probably myself and some others around the

table are asking, can you summarize for us the adequate other treatments?

DR. COMO: Are you talking about the other pharmacologic treatments?

DR. YANG: Correct.

DR. COMO: Yes. Other than the trial of clomipramine, the four trials of naltrexone and, of course, the studies that were conducted by the sponsors to get the expanded indication for those two drugs, the majority of the other pharmacological studies that we reviewed were again limited by small case series or single case reports.

And as Dr. Park mentioned in his presentation, some studies -- well, with the pharmacological studies, they do have a tendency to report adverse events. And, again, as I mentioned, the adverse event profile did not seem to be different than for the approved indications of those off-label drugs, nor were children with intellectual or developmental disabilities appearing to be at a higher risk for developing AEs.

DR. YANG: Yes, we understand the limitations of what's out there, so we appreciate you trying to put it all together.

DR. COMO: Sure.

DR. YANG: Are there any other questions from the Panel for FDA before we start the questions for JRC?

Yes, Dr. Peavy.

DR. PEAVY: Guerry Peavy.

I think it was some parents that brought up the issue of puberty and things getting worse, the symptoms getting worse around that time.

Dr. Como, did you find anything that had anything to do with developmental stage or age? Because there are lots of differences there, and there could be some reasons for differences in response to treatment.

DR. COMO: That's a very simple quick answer. No.

DR. PEAVY: No, okay. I thought it would be.

DR. YANG: Okay, last call for questions for FDA from the Panel.

All right, why don't we go on to questions to JRC, then. Thank you FDA.

Dr. Connor, would you like to address -- and also, could the representatives from JRC please come closer to the podium?

DR. CONNOR: Thank you. Jason Connor.

So a very quick question and then hopefully a not much longer question. One of the videos we saw, and it showed the student receiving the shock -- basically, his knees buckling. So one of the questions we're talking about is we are hearing there are not adverse events or limited adverse events. So are there records of injuries that people sustained if they fall or flip back or whatever, in response to a shock?

DR. YANG: Dr. Connor, I think they were all moving up to the front.

DR. CONNOR: Oh, okay.

DR. YANG: So you may want to quickly restate.

DR. CONNOR: Okay, I'll repeat that. So in the video, we saw a student receive a shock, and he went down to his knees, and there was a table there and he didn't hit the table. But we're hearing that there are no adverse events.

Is there a history of any adverse events of someone cracking his head on the table because he falls when he's shocked, or flipping back and hitting his head on a wall when he's shocked? Because there seems to be physical reaction to receiving the shock. You know, I once shocked myself fixing my kitchen, and I fell down. That's my question.

DR. BLENKUSH: What you saw, that's not what normally happens. I mean, I give --

DR. CONNOR: I'm not asking what normally happens.

DR. BLENKUSH: Oh.

DR. CONNOR: Is there any history of injury?

DR. BLENKUSH: No. I mean, not that we're aware of. I mean, we keep records of all their medical records. We have databases; we have all of this information.

DR. CONNOR: Okay. So no one has been injured in response to, like, their physical reaction after receiving shocks?

DR. BLENKUSH: I mean, I've been there for eight years, and I don't have any experience or any record --

DR. CONNOR: Okay.

DR. BLENKUSH: -- of any of my -- the people that I work with having been injured as falling.

DR. CONNOR: Okay, that's good. Thanks.

DR. BLENKUSH: Yes.

DR. CONNOR: So then, my next question -- you can stay there. You know, patients who don't respond to all of these other therapies -- and I understand that you're getting extremely hard-to-treat cases that have been kicked out of other very reputable programs.

Why does this work? Meaning, patients who have this behavior, they get restrained, they get sequestered, there are all of these things that presumably aren't pleasant that don't work. Why does this work? And maybe that's too hard a question to answer here. But what is fundamentally different? Because it sounds like -- I mean, you said 100% efficacy of dropping below 90%. That's amazing when nothing else works. What's the mechanism?

DR. BLENKUSH: So there's a lot of behavioral principles involved. And this comes from basic research in operant conditioning that's been conducted for many, many years with humans and animals. And the first thing is that the immediacy of the consequences is essential, okay? So the behavior occurs, and then there's immediate presentation of the consequence.

Now, a lot of the other procedures that are used as punishers or things to decrease behaviors, the problem is that they come far after the behavior occurred, okay? So that's one disadvantage of things like timeout and even -- and the other thing is that there's very little chance that the person can avoid the stimulus.

Okay. A lot of times, if you see physical restraints happening as consequences, it's very hard to implement a physical restraint with someone who's 200 pounds. I mean, I'm sure that many of you have seen this in emergency rooms and other things. I mean, a person who is 200 pounds comes in and they're attacking people, and you try to contain them physically. It's not easy to do. And so there's a lot of avoidance responses that are negatively reinforced.

And then the other thing is that most people aren't -- it's a unique stimulus. You don't come into contact with the GED consequence very often, and you don't -- it's a unique stimulus. So that's another property of it that we think adds to it.

And the other thing is that, compared to a lot of other stimuli, it doesn't linger. When you use, like, ammonia and taste aversives, those can linger in the mouth for extended periods of time.

So let's see. Those are probably the main reasons, I would say.

DR. CONNOR: Okay, thank you.

DR. YANG: Mr. Mikita, you have a question?

MR. MIKITA: Just a couple. Thank you.

Is it your testimony before this Panel that in your experience using these aversive devices, that you've never had staff file one incident report noting an incident of an individual falling or hurting themselves as a result of the application of this device? Yes or no.

DR. BLENKUSH: In my experience at JRC, I've not seen records that suggested that happened. Yes.

MR. MIKITA: Okay. And what is JRC's opinion of patients and staff who have either administered these devices to patients or the patients who have received them and who have described in particular detail the pain, the anxiety, the fear, and the horror that they experienced as a result of this remarkably helpful treatment that JRC purports to provide to this subset population who cannot be treated anywhere else in the country without the device?

DR. BLENKUSH: So, unfortunately, I can't describe or talk about former patients. If they would provide consent, I'd love to provide and discuss the individual cases. And if those people would like to do that, we'd be more than happy to do that, to see a complete record of their treatment history.

But, look, every treatment -- nothing's perfect, right? There are side effects to lots of things, and there are advantages and disadvantages. And what we want people to do and what we really want everyone to look at

is let's really weigh the risks and the benefits of these treatments.

You know, we were talking about medications before, and I know that we were talking about some of these dependent variables in some of these studies. The aberrant behavior checklist is a very poor description of severe problem behaviors. It has 15 items, and only three of them have anything to do with aggression and self-injury. So when you see these effects, the mean scores in these studies are like a change from like 30 -- and again, this is a four-point rating scale -- 30 to 22. I mean, these are very small effects.

And the side effects of these drugs, which I'm sure all of you are aware of, those are -- so when you look at risks and benefits of treatment -- you know, we're open to any scientific process. We're open to having this device investigated. We're open to using it and having it involved in studies. And we would love to do that. We just haven't had a chance to do that recently.

DR. YANG: You had one more question?

MR. MIKITA: One more question. I want you to just very briefly describe the court procedure.

(1) Are the court hearings allowing -- is it held by the same judge in Massachusetts, or is it a rotating panel of judges? (2) Is it the same attorney or guardian ad litem who is providing legal counsel? And is notice sent out to other family members every time that a hearing is convened?

And (4) is the hearing taking place at the JRC or is it taking place in a courtroom?

DR. YANG: Mr. Mikita, I'm going to interrupt here, because I think this is a bit outside of the scope of what we are here to talk about and to discuss in terms of ESDs.

DR. BLENKUSH: I'm happy to answer the question.

DR. YANG: So I will defer to Dr. Peña as to whether or not. To me, this is procedural.

DR. PEÑA: Right, I would focus on --

MR. MIKITA: Well, it goes to the vulnerability of these patients. And if we're talking about harm, it goes to consent. And if they're incapacitated and vulnerable, I think it's very relevant.

DR. YANG: I think we understand that these are vulnerable patients.

DR. BLENKUSH: I'd love to answer the question, I really would.

DR. YANG: I think we will pass on that.

DR. BLENKUSH: Okay.

DR. YANG: But thank you.

I do have a clarification. So let me ask a clarification to follow up on a couple of these questions. So there has been no patient, that you know of, that has had to seek hospitalization or outside medical care as a result from these ESD treatments; is that correct?

DR. BLENKUSH: Well, I said, of the people that I treat, the people that are on my caseload that I've worked with over the years, no, they haven't gone to the hospital because of the GED. No.

DR. YANG: Because of the sequelae of the GED?

DR. BLENKUSH: No.

DR. YANG: What about the others that have been treated?

DR. BLENKUSH: Again, the program is 40 years old. I'd have to go back and review. I don't know. I only have a certain caseload.

So do you want to answer that?

MS. CROOKES: Yes, I can answer that. There has been -- when we had the incident with the hoax in 2007, we sent two of students to the hospital for evaluation after the inappropriate use of the device. I've been there for 24 years, and those are the only two times that that's happened.

DR. YANG: Okay, thank you for the clarification. Hang on one second.

So we have Drs. Fost and Armstrong, and I'll put these two down.

DR. FOST: Norm Fost.

A brief question. The Fox video. Dr. Blenkush or anybody else from JRC, do you have a comment on that? That showed the individual that was restrained and seemed to be shocked a large number of times that seemed to some people excessive. Do you have a comment on that?

MS. CROOKES: Dr. Blenkush stated previously, I believe, that that was a very rare instance. Andre had done very well at JRC. He had received a total of 26 applications in the two years he was on the GED device. That day, his treatment did not work, for whatever reason. He had had some issues on a previous home visit. He came back a little bit different than he had before he left and the treatment didn't work. The doctors that were in the room, the nursing staff, determined much later than would have happened today -- that was 12 years ago -- that the treatment wasn't working and the treatment stopped, and he was sent for an evaluation after his behaviors had changed.

DR. YANG: Thank you.

UNIDENTIFIED SPEAKER: That's a lie.

DR. YANG: I'm sorry. Let's go on to Dr. Armstrong.

DR. ARMSTRONG: Two quick questions. One is we received in our panels a list of patient-by-patient descriptions of adverse events, and they almost all said none. And we had received information from patients and testimony here that had described a number of adverse events, including things that weren't listed in the consideration. It sounded like neuropathies and paresthesias that last for a long period of time.

Why are we seeing this big difference between the report from patients who have been through the process and the data that were submitted?

MS. CROOKES: The information that you received, we don't know who was interviewed or who reported that. What we reported on in our packet was what we know of the current clients that are on use of the device and the adverse effects. If those effects are not reported to us when the student was in the program -- and certainly none of those that testified here today had reported any of those side effects to us.

DR. ARMSTRONG: Okay. My second question really gets down -- we received, a few minutes ago, the user's manual on the device, and there are a couple of things in there that are concerning. One is there is a specific statement: This isn't used in water. But we've heard testimony that people received shocks while wearing it in the shower, while getting wet.

And the second component of that. It has been raised that these are good operant conditions. But non-contingent shock, because of the failure of the mechanism to apply shocks to the wrong people at the wrong time, really sort of violates in a big way the operant principle. So can you discuss those misuses, according to the guidelines and the malfunctions?

MS. CROOKES: The device is never worn in the shower. The device was worn on an arm that was outside of the shower, cuffed out. And that was only done in cases where the students would exhibit severe behaviors in the bathroom. So at no time was the device wet or immersed in water. It was covered.

That has changed. I believe in 2011, 2010, that policy was

changed, that they no longer wear anything in the shower. It's a prototype device, like a phony device. So if we feel that they may realize they're not wearing it when they're in the shower, they'll wear that. But no student wears an active device at all in or out of the shower.

DR. ARMSTRONG: Okay, what about the malfunction?

MS. CROOKES: Nathan can probably answer that better than me.

DR. BLENKUSH: Again, this is something that does happen from time to time. There's something called spontaneous activations. There are staff who make mistakes on rare occasions. So I'm just being told that we had six spontaneous activations in a year.

Okay. So considering that we have 60 people that are receiving treatment, it's a very low probability. And yes, it's something we don't want to have happen and something we want to avoid. And we do things. The devices are calibrated; they're monitored. There are checklists that our electronics department goes through to make sure the devices are maintained. They go through a process where we evaluate them. So all of that stuff happens, and we do everything we can to minimize that.

DR. ARMSTRONG: When those events occur, are they reported to the state as significant events? If a drug batch went wrong, there would be state reporting, in almost every state, of that malfunction. Does that occur when that happens?

DR. BLENKUSH: Yeah, yeah. It is reported, yeah.

DR. YANG: Dr. Miles.

DR. MILES: It would seem to me that if you had six discharges in a year of a therapeutic device, Class II device, that you're using in your facility, we should be seeing six reports a year coming out of your facility in the MAUDE database. I went through the MAUDE database, and I don't see those. Are you reporting or not?

DR. BLENKUSH: I'm not involved in that process.

MS. CROOKES: Back in the review -- I don't know if it was 2000 when we were reviewing this -- we were told by FDA that spontaneous activations and misapplications were not reportable.

DR. MILES: Excuse me, that is a precise fit to the FDA definition of a malfunction. I don't believe you.

MS. CROOKES: Oh, okay, okay.

DR. YANG: Okay, I think we better stop on this line of questioning.

Dr. Goodman, do you have a follow-up to the same topic, or is this a new question?

DR. GOODMAN: It's a new question.

DR. YANG: Okay, can you hold, then, because we have two -- a few others before you, then? Okay.

So Dr. Stebbins.

DR. STEBBINS: Glenn Stebbins.

So you already said this, but I wanted to just clarify again. How many patients are currently receiving the GED treatments? And they are the only ones who will from now on, according to Massachusetts law? And is there any estimation of how long that treatment will last?

DR. BLENKUSH: So the first thing is that the information that was presented, that Massachusetts passed a law that prohibited JRC from using GED, is not true. JRC has a settlement agreement in place right now, and we are able to use GED as long as we have court approval to do so. We've even submitted a plan for approval to the court recently. So that's the answer to the first question.

Okay. And the second question --

Okay.

DR. YANG: Okay, thank you.

So let's move on, then, to Dr. Bickel.

DR. BICKEL: When you talk about applications of the device, does that -- every time you talk about application, is that one two-seconds-or-less application, or is that a bout of shocks?

MS. CROOKES: An application is one two-second shock. It's not less than two seconds, and it's not more than two seconds. It's a single two-second shock.

DR. BICKEL: And could you give me again the range of the

applications that a person would receive in this treatment?

MS. CROOKES: For?

DR. BICKEL: You know, let's say in the course of a standard month, someone might receive at the high end X number, low end --

MS. CROOKES: The current range is 0 to 39 in a week for the last six months.

DR. YANG: Let me remind the public attendees that they may not participate in this session of Panel deliberations.

So let's move on to Dr. Dorsey.

DR. DORSEY: How is an individual supposed to report an adverse event? If they experience paresthesias and numbness, how is that supposed to be reported after they received a shock?

DR. BLENKUSH: Again, everyone sees the nurse within 24 hours after a shock, so they could report it then. They could talk to us, they could talk to the staff, they could do all of those things. It's through the process.

DR. DORSEY: Does a nurse ask them any question like they would in a pharmaceutical study: Have you had an untoward occurrence from the shock?

DR. BLENKUSH: I don't think that's part of the assessment. I think they go there and they check the skin. They might just do -- I don't know the complete extent of the assessment.

DR. YANG: Okay, we have approximately 10 minutes, so let's

do Ms. Mattivi. I'm being told five minutes. Ms. Mattivi and then Dr. Goodman and then Dr. Weigle.

MS. MATTIVI: I've got a quick question. Kris Mattivi. I'm the Consumer Representative.

In the warning section of the user manual, it says it's to be used only by or under the direct supervision of a licensed professional. Can you tell me how that's being operationalized?

DR. BLENKUSH: So every plan, we design a comprehensive behavioral program. It has components that include differential reinforcement, it has components that have to do with anesthesia interventions, and it has components that have to do with consequences for behavior. So all of our staff receive instructions and training on how to follow our program. And this program is spelled out on the recording sheets that accompany the student everywhere they go.

So whenever I make a change to a differential reinforcement procedure, there are changes that occur on that sheet, and the staff are instructed to follow that plan. And the same is true with a GED consequence. If we change a consequence for a behavior, then that's very clearly listed on the plan, and the staff are instructed to follow it.

MS. MATTIVI: So a licensed professional is not necessarily directly supervising the use of this device?

DR. BLENKUSH: Well, again, we have board certified behavior

analysts and licensed psychologists that compose and monitor the plans.

DR. YANG: Dr. Goodman.

DR. GOODMAN: A technical question. Before I was a psychiatrist, I was an electrical engineer, so I'm going back to a technical point here.

It was mentioned earlier that this is a DC device and there are advantages of a DC device over an AC device in terms of tolerability and safety. But, in fact, when you look at the user manual, you may be starting with a DC current, a battery, but it's being converted to an oscillatory waveform. It's a square wave, high-frequency square wave, high voltage. So I think it's a bit misleading to represent this as a DC current. It's not like it's going to -- because it is a complex pulsatile waveform.

DR. YANG: Does anyone from --

DR. GOODMAN: Would anybody agree or disagree with that characterization?

DR. YANG: Would anyone from JRC like to address that?

MS. CROOKES: I don't think any of us are in a position to answer that.

DR. CONNOR: Jason Connor.

I think this may actually refer to the old device, and the new device might actually be DC, which is part of the problem. I don't know, but my guess is it might be.

MS. CROOKES: It is. And we had submitted all of that in the documents.

DR. GOODMAN: And that's a pure DC waveform, not alternating, not square wave?

MS. CROOKES: I don't want to answer that without --

DR. GOODMAN: Okay.

MS. CROOKES: -- being sure.

DR. YANG: Dr. Stebbins for a follow-up.

DR. STEBBINS: Is there an updated manual?

MS. CROOKES: What year do you have?

DR. STEBBINS: We have the one from GED-1.

MS. CROOKES: Oh, yes. Yes, absolutely. We update that every time that a procedure is changed.

DR. YANG: Does the FDA have a copy of that?

MS. CROOKES: Yes.

DR. YANG: And is that something that can be distributed during the break?

DR. PEÑA: I can confer with the team on this.

DR. YANG: Okay, very good. Thank you.

Do you have an updated copy?

MS. CROOKES: Not with me, no.

DR. YANG: Okay. Okay, Dr. Weigle, did you want to go ahead

and ask -- no, okay.

Are there any other Panel questions for JRC? Keep them short.

DR. CONNOR: Absolutely.

DR. YANG: We're heading for the break.

DR. CONNOR: So it's just still unclear to me. Can a new patient at JRC go to court and be started on this device?

DR. BLENKUSH: Yes. Again, we have --

DR. CONNOR: Okay. No. Yes was all I needed to clarify. Thank you.

DR. YANG: Thank you.

Do you have a question? Is it a follow-up on that or a new question?

DR. BICKEL: A new question.

DR. YANG: A new question. Hold on.

Dr. Dorsey.

DR. DORSEY: I just want to follow up on Ms. Mattivi's question. So the GED device is currently used, at times, not under the direct supervision of an appropriate licensed professional?

DR. YANG: JRC, could you please confirm or deny?

MS. CROOKES: No, it's under the supervision of the licensed -- not direct observation.

DR. DORSEY: The warning in the indication is the GED should

be only used by or under the direct supervision of an appropriate licensed professional. Is that occurring all the time? Yes or no.

MS. CROOKES: No.

DR. DORSEY: Why? Why aren't you following your user manual?

MS. CROOKES: That's not our current user manual. Our user manual -- a lot had changed with FDA in 2000 when we were told we were no longer under the 510(k) process. Since 2011 when they changed their minds, we've been working with them. We've submitted a new pre-submission, a new user manual, new documents. We hired a company to develop a new device. So there has been a lot of changes since then.

DR. DORSEY: Thank you.

DR. YANG: Okay. Is it possible for JRC to be able to get a copy of that manual so that we can have it during the break?

MS. CROOKES: I can see if someone can send it over, yes.

DR. YANG: Could you please send it to Avena Russell?

MS. CROOKES: Yes.

DR. YANG: Okay.

MS. CROOKES: One of my associates is going to try to have it sent.

DR. YANG: All right. Then we have, I believe, Dr. Bickel.

DR. BICKEL: I was wondering, do you have the device with you

and could any of us sample it?

MS. CROOKES: We did not bring a device, but if you come to JRC, we'd be happy to show you.

DR. YANG: Thank you.

So let me just ask one more time. Any other brief questions for JRC from the Panel?

Okay. If not, since this has been extended deliberations, when we come back from the break, we will go ahead and go right into the Panel questions, where we will go around the table and around the Panel members to survey the Panel members in terms of their answers to the questions.

So at this point again, for the break, I'll remind you to please do not contact anyone -- this is to the Panel members -- about the meeting topic during the break, and this includes discussion amongst yourselves or with any members inside or outside the audience.

Let's now take a 15-minute break and reconvene promptly at 4:10, where we will begin with the Panel questions.

(Off the record.)

(On the record.)

DR. YANG: Okay. So now that we're all back from the break, we will now proceed with the FDA questions.

To the Panel members, copies of the questions are on the yellow sheets that are in your folders. I would ask that, again, for

transcription, please identify your name before you give your comments.

Also, just a couple of things: As Dr. Bowsher asks the question individually, I will be going around the panel table. Please first answer the question yes or no. Actually, answer the question, and then take a minute or less to state your concerns or any comments that you have about the question.

Also, I am to read that to please keep in mind, when making your response, that FDA is considering the issue of proposal to ban a class of devices, the aversive conditioning electrical stimulation devices that are intended to administer a noxious electrical stimulus to modify undesirable behavioral characteristics in patients who exhibit self-injurious behavior and aggressive behavior. Section 516 of the FDA Act authorizes FDA to ban a medical device that presents "an unreasonable and substantial risk of illness or injury based on all available data and information."

So with that, Dr. Bowsher, if you would proceed with Question 1, please.

DR. BOWSHER: Sure. This is Kristin Bowsher.

Question No. 1: In assessing the reasonableness of the risk of illness or injury posed by a device, FDA considers the availability of other treatment options including pharmacological, behavioral, alternative, and experimental therapies for the treatment of SIB and aggressive behavior.

a. In general, do you think these other treatments are adequate

to address SIB and aggressive behavior?

b. Is there a specific subpopulation of patients exhibiting SIB and aggressive behavior for which these options are inadequate?

DR. YANG: Dr. Bowsher, if you don't mind, I think it may be more efficient if we take 1a and proceed around, and then we'll come back with 1b.

DR. BOWSHER: Sure.

DR. YANG: So, I'm sorry, I have to start somewhere.

Dr. Kim, can we -- oh, no. I'm sorry.

So if you could first tell me the answer to the question, the exact question, do you think that these other treatments are adequate to address SIB and aggressive behavior? If you can state a yes or no and then tell me any concerns within a minute, that would be great.

DR. KIM: I think the answer is, to my mind, obviously no. If it were, we wouldn't be here. I think that there are many therapies that have effect. We just don't have data to know which work when for whom. I think the idea of defining refractory serious self-injury and then saying if it works with this treatment for that group, that person, it should be good for everybody in that group is a mistake.

I mean, just as a psychiatrist, we often have cases in which you could try a number of things for the same type of severity, it doesn't work; you've got to try something else. So I think that, especially for medications

that have significant burdens, I think it's pretty clear.

DR. YANG: Thank you.

Dr. Stebbins.

DR. STEBBINS: Glenn Stebbins.

I would say yes, in general. My concerns are, though, that we don't really have enough information on long-term efficacy in specific subgroup applications.

DR. YANG: So we'll save that subgroup to the next one, too.

Okay, Dr. Peavy.

DR. PEAVY: I would say no. I think that Dr. Kim expressed it so well that I probably don't need to comment. I would agree completely with what he said.

DR. YANG: Thank you.

Dr. Augustine.

DR. AUGUSTINE: Erika Augustine.

I also would say no. While for the majority of individuals with self-injurious behaviors and aggressive behaviors, it's likely that these other treatments are at least partially effective, there clearly are some who are not going to be responders.

There was a question earlier about the responder rate for the risperidone and the aripiprazole studies, and I was able to, at least for one of those, find a responder rate which still wasn't specifically about SIBs and

aggressive behavior; but in terms of irritability and CGI, there was a 69% responder rate in the risperidone group. That was in the study that had 101 patients compared to 12% in the placebo group.

So even with that being sort of a broad measure of irritability and not even this very specific symptom that we're delving into, there's one example of where treatment is incomplete.

DR. YANG: Thank you for those details.

All right, Dr. Connor.

So the question -- again, I'd like to restate the question every few Panel members that, do you think these other treatments are adequate?

DR. CONNOR: No. I mean, it's clear there are plenty of refractory cases, and the situation we're hearing about is sort of the most highly untreatable cases. You know, the risperidone trials are small, they're short-term, and here we're asking about long-term effects. We know nothing about long-term effects of other ones. We've talked about adverse events. Thirty-three percent of patients, even in an eight-week trial, gained over 7% of their body weight. A 150-pound person, that's gaining 11 pounds in eight weeks, you know, for alternative therapy. So there are definitely adverse events. And it certainly helps some, but I think there is clearly an important part of the population that other methods aren't treating.

DR. YANG: Thank you, Dr. Connor.

Mr. Mikita.

MR. MIKITA: I will say yes. I believe that, on a case-by-case basis, patient-by-patient basis, that there is enough available therapies in this country. I think that they are treating individuals throughout this country and states, not sending individuals to places like JRC, that are effectively treating these individuals, and I represent some of those agencies that do.

DR. YANG: Thank you, Mr. Mikita.

Dr. Goodman.

DR. GOODMAN: Wayne Goodman.

No. Based upon my understanding of the literature and personal clinical experience, particularly in Tourette syndrome with self-injurious behaviors, some of whom I've evaluated for deep brain stimulation, which it, too, has been hit or miss in treating the target symptoms, there's clearly a treatment gap for some patients with refractory self-injurious behaviors and aggression, and that's despite the best available behavioral and medication treatments individually or in combination.

DR. YANG: Thank you, Dr. Goodman.

Dr. Miles.

DR. MILES: Steve Miles.

The existing drugs and treatment programs are partially effective, but more importantly, they are under active research using standard comparison group prospective research designs. However, the fact that the above therapies are not completely successful or don't work on all

patients does not mean, therefore, that electrical aversive stimulation is indicated. Any indication for such devices must be predicated on an assessment of the efficacy of that therapy's efficacy and risk.

DR. YANG: So just to clarify, do you think that the other treatments are adequate to assess SIB and aggressive behavior, yes or no?

DR. MILES: Partially effective.

DR. YANG: Partially effective, okay.

All right. Dr. Bickel.

DR. BICKEL: Warren Bickel.

I do not think that the other treatments are adequate. First off, as it was addressed, there's not a lot of data to address this, in general, and that's concerning. And, secondly, it's unfortunately rare that any treatments in psychiatric or behavioral issues are universally effective. So I don't think these existing treatments work. On everybody.

DR. YANG: Thank you.

Dr. Armstrong.

DR. ARMSTRONG: The important question is "in general," and the answer is yes.

DR. YANG: Okay, thank you.

Dr. Dorsey.

DR. DORSEY: Ray Dorsey.

No, for the reasons stated by the other panelists.

DR. YANG: Okay.

Dr. Fost.

DR. FOST: Norm Fost.

No. Just to repeat the reasons for the no, we've heard testimony from numerous families, read others in the material submitted. There are clearly lots of people out there who have tried very hard to seek effective therapies and it doesn't work; whether that's due to incompetent therapists or people aren't trying all the right things, I don't know. But then I hear from Dr. Goodman and others on the Panel who are experienced, who say even when you use all the best stuff, it doesn't always work.

Second, even when it does work and possibly ameliorating the behaviors, there are adverse effects that may be unacceptable, and these aren't great drugs in that regard. So it seems to me there's clearly a need out there for less toxic, effective therapies for a considerable number of patients.

DR. YANG: Thank you, Dr. Fost.

Dr. Weigle.

DR. WEIGLE: Hi. Karen Weigle.

I'm having a hard time between the yes and no, as well.

DR. YANG: You join Dr. Miles and the "partially"?

DR. WEIGLE: Yes. I had yes and no both written here.

Because I think, like Dr. Armstrong said, in general, yes. We have a lot of technologies and not just what's listed here, but other things

including ensuring that medical and psychological factors are adequately addressed. If you consider all of those aspects -- of the person as well as quality of life -- oftentimes even for those people who are considered refractory, are the most difficult to treat, can be treated successfully. And usually are, in time, in my experience. So I guess that leaves me just with yes, not a no.

DR. YANG: All right, that's what I'll change you over to.

Okay, Dr. Green.

DR. GREEN: Okay. My answer is no. I mean, I'm not surprised that the behaviors that we're trying to treat is a final common pathway of a variety of underpinnings which we may or may not easily expose and, therefore, one is always going to see mixed results. And so the answer is no.

DR. YANG: Thank you, Dr. Green.

Dr. Iwata.

DR. IWATA: No. I'm confident that I've treated more people with self-injurious behavior than anyone in this room. Nevertheless, I can't add anything to what Dr. Como mentioned in his review of the literature, which was very clear that nothing works all the time.

DR. YANG: Thank you, Dr. Iwata.

Dr. Richardson.

DR. RICHARDSON: No. If there was, we wouldn't be here.

DR. YANG: Thank you.

Ms. Mattivi.

MS. MATTIVI: Also no for the reasons that have been previously stated.

DR. YANG: Dr. Reppas.

DR. REPPAS: John Reppas.

No. There is a substantial unmet need here.

DR. YANG: Okay.

So, Dr. Peña, the majority of the Panel generally believe that no, these other treatments are not adequate to address SIB and aggressive behavior. We did have one-third -- sorry -- approximately 25% say yes, in general, with qualifiers.

And these are the qualifiers: That there seem to be many therapies, but really no data to support them; there's no data on long-term efficacy; there are many documented refractory cases; the adverse events for these other therapies are not well defined, but at least they are under active research; there are many diagnostic ideologies, and this may be the final common pathway for some of these diagnoses; and certainly for some of these diagnoses, these other treatments do not seem to be adequate.

And I must add that we had one "partially."

DR. FOST: Just one correction of that summary. You said the adverse effects of other therapies aren't well defined. I think some of them are very well defined, and the problem is that they're problematic.

DR. YANG: Well stated. Thank you for the clarification.

Dr. Peña, is that adequate for 1a?

DR. PEÑA: Thank you for summarizing for 1a.

DR. YANG: Okay.

Dr. Bowsher, would you tell us 1b again?

Or shall I just -- go ahead.

DR. BOWSHER: Is there a specific subpopulation of patients exhibiting SIB and aggressive behavior for which these options are inadequate?

DR. YANG: So Dr. Reppas.

DR. REPPAS: I won't be nearly as eloquent to start off.

So by definition -- because I said no to 1a, the answer here is yes. I'm not smart enough to define that population, however.

DR. YANG: Okay, thank you.

Ms. Mattivi.

MS. MATTIVI: I would also say yes, and certainly out of the realm of my information and expertise to talk about what that subpopulation might be.

DR. YANG: Thank you.

Dr. Richardson.

DR. RICHARDSON: Yes. Unfortunately, I'm in the position of seeing a lot of the failures come in and ask for something to be done.

DR. YANG: Dr. Iwata.

DR. IWATA: Yes.

DR. YANG: Dr. Green.

DR. GREEN: Yes, it's just those refractory to what's called the more conventional therapies.

DR. YANG: Certainly, Dr. Weigle, before you start, if you do have a suggestion for what the subpopulations are, especially those of you that treat these ongoing, please do state what those might be.

So go ahead. Dr. Iwata, do you want to do so?

DR. IWATA: Well, there are no predictor variables to tell for whom any given intervention may or may not be effective.

DR. YANG: Okay.

DR. WEIGLE: I guess I would say yes, there is a subpopulation. I think there are a couple of groups of people who are less likely to respond to some of the other treatments or any treatments, possibly. Maybe those with very specific genetic disorders where there are very specific behavioral phenotypes and outcome symptoms related to that, for example Lesch-Nyhan or something. And for whatever reason, a lot of people on the autism spectrum are somewhat susceptible to engage in self-injury more frequently than others.

DR. YANG: Thank you.

Dr. Fost.

DR. FOST: Norm Fost.

There most certainly are subpopulations. I just have no idea what they are. I don't think we heard enough data to know about that. More research about that might be helpful.

DR. YANG: Thank you.

Dr. Dorsey.

DR. DORSEY: Ray Dorsey.

Yes. Especially concerned about those with self-injurious behavior.

DR. YANG: Dr. Armstrong.

DR. ARMSTRONG: Yes. I was short last time. I'll be a little longer this time.

I think the reason that we are in this position is that we do not have the way to adequately identify the subpopulations, what the parameters of those might be. In the cancer area, we are moving to increasingly individualized therapy. Here, we're in an umbrella that says somebody walks in with this behavior, and we know that these behaviors have multiple pathways, and so until we are able to better discriminate and define not just on the basis of a self-injurious pathway, but what is happening on an individual level -- then we have subpopulations. The treatments may work, but we have not yet figured out how to match them.

DR. YANG: Thank you, Dr. Armstrong.

Dr. Bickel.

DR. BICKEL: Yes.

DR. YANG: Thank you.

Dr. Miles.

DR. MILES: Yes. But I don't know what they are.

DR. GOODMAN: Yes.

Wayne Goodman.

DR. YANG: Okay.

Mr. Mikita.

MR. MIKITA: Yes, for the same rationale of Dr. Fost and Dr. Miles.

DR. YANG: Thank you.

Dr. Connor.

DR. CONNOR: Jason Connor.

Yes, I agree. And I agree that I think it's ill defined who they are.

DR. YANG: Dr. Augustine.

DR. AUGUSTINE: Erika Augustine.

Yes for the reasons that have been stated.

DR. YANG: Dr. Peavy.

DR. PEAVY: Yes. And I think probably these groups will be composed of a combination of factors, things like age -- could be. The level of

cognitive impairment, developmental stage. Genetic disorders was mentioned.

DR. YANG: Thank you.

Let's see here. Dr. Stebbins.

DR. STEBBINS: Glenn Stebbins.

Yes. And for all the reasons stated.

DR. YANG: And finally Dr. Kim.

DR. KIM: I have nothing to add. Yes.

DR. YANG: Okay.

All right. So with regard to Question 2, Dr. Peña, it is unanimous amongst the Panel members that there seems to be a specific subpopulation of patients exhibiting SIB and aggressive behavior for which the above options are inadequate.

However, it is also the general consensus that these populations are ill defined except for perhaps some suggestions for specific genetic diseases with specific phenotypes like Lesch-Nyhan, also maybe for some of the autism. There are no predictive variables, and it's very difficult to define these subpopulations with what we have now, so more research is needed.

Dr. Peña, is that adequate for Question 1b?

DR. PEÑA: Yes. Thank you for summarizing the sense of the Panel.

DR. YANG: Dr. Bowsher, Question 2a.

DR. BOWSHER: When determining whether the risk of illness or injury posed by a device is substantial, FDA will consider whether the risk is important, material, or significant in relation to the device's benefit.

a. Please discuss whether available evidence presented at this panel meeting demonstrates that ESDs that are intended to administer a noxious electrical stimulus for the modification of SIB and aggressive behavior provide benefit. If so, please identify any specific population of patients for which effectiveness has been demonstrated.

DR. YANG: Okay. I think we'll start with Dr. Armstrong and go around to my left.

DR. ARMSTRONG: So this is not a yes/no? This is --

DR. YANG: Well, let me restate then.

So, first of all, there is a yes/no question. There is do the available evidence presented at the panel meeting show that there is a benefit? So that's the yes/no.

And then if the answer is yes, then what subpopulation, if you can define it.

DR. ARMSTRONG: It's still a very difficult one to say yes or no. We have heard reports from patients and from family members that, for them, there was a benefit and so on. An anecdotal report, yes, there is a

benefit. We do not know how to identify that subpopulation, who will benefit, nor do we know how to identify the population who may be at greater risk who may experience significant difficulties.

DR. YANG: Okay. Thank you very much.

Dr. Dorsey. So, again, there is a buried question in this and that is does the evidence presented here today show that these devices have a probable benefit?

DR. DORSEY: No, it does not. The benefit of the electrical stimulation devices is really uncertain, largely because of the low quality of evidence. We've heard moving testimonies and case reports of individuals who have benefited greatly from the device, and individuals who report that not only they didn't benefit, but that they actually had harm as a result of the device. And just the quality of the evidence is quite poor.

To my knowledge and reading the materials, there hasn't been a single randomized study, there hasn't been a single blinded study, there hasn't been a single study that employed an independent rater, there hasn't been a single prospective study, there hasn't been a single study that has used a pre-specified income and a pre-specified outcome. There hasn't been a single multi-center study. There's only been one study that used a control or comparison group. There are ways that we can advance knowledge, and we have those tools in 2014, and to date, we have decided, for whatever reason, not to use them. And because we haven't, we can't answer this

question. So no, there's no evidence at the present time.

DR. YANG: Thank you, Dr. Dorsey.

Dr. Fost.

DR. FOST: Norm Fost.

Yes, I think there is lots of evidence. We've heard it today from the parents and from respected, well-trained physicians. It's not great evidence, it's not gold standard evidence, it's not a randomized controlled trial, but I must say I'm troubled by the catch-22 of people who say, well, we don't have evidence, but we certainly shouldn't do randomized trials, that there is some regulatory or ethical barrier to doing studies. I don't agree with that. It's important to do those, as it is for all interventions.

As everybody knows, a substantial amount of clinical practice is not subject to well-designed studies, but we don't ban things. And they have adverse effects, and much of standard practice has way more serious adverse effects than what we've heard about today, and we don't ban things because of that, so much better evidence is needed. I think there's enough evidence to justify going ahead with a well-designed trial.

DR. YANG: Dr. Fost, I just want to clarify. So yes, I understand the limitations with which you say that yes, there is a probable benefit. So are you willing to speculate on the subpopulation that might have benefited?

DR. FOST: As before, I have no idea --

DR. YANG: Okay.

DR. FOST: -- what the subpopulation is that would benefit.

DR. YANG: Okay. Thank you very much.

Dr. Weigle.

DR. WEIGLE: Hi. Karen Weigle.

I think that I'm going to have to say no because of the same reasons that Dr. Dorsey talked about with regard to the quality of the data that has been provided. And everybody keeps asking about why haven't well-controlled studies been done, and what's holding that up. And I think it's kind of like the elephant in the room, is that it's considered tortuous to the majority of communities around the world to shock people, to use aversive conditioning on human beings. And I think that have we tried this with alcoholics or people who smoke since 1976? Haven't seen that application either.

So I think that what has happened is that this has gone on for this long because this is a population who cannot adequately speak for themselves, either physically because they're nonverbal or they just don't have the capability or the position to be able to report adverse effects and outcomes until they're gone and then they come back. But when they're in the situation, at least some of the people here today did not report adverse effects when they were having this treatment, probably out of fear, which, in and of itself, to me, presents a problem with the use, period.

DR. YANG: Take your points there.

Dr. Green.

DR. GREEN: We have anecdotal evidence to support benefit to alter a particular behavior. I think the question is at what price? And we don't have any ability to do a risk/benefit analysis because we really have little ability to recognize the psychological end, the risks, in a nonverbal population, particularly.

DR. YANG: Thank you, Dr. Green.

Dr. Iwata.

DR. IWATA: Brian Iwata.

Yes. This is a population for whom it will be difficult, if not impossible, to do any of the kinds of research that has been suggested because these individuals are only considered for this treatment if all the other treatments fail. So it's not surprising to find that the available research does consist of case studies or small case series. If you look at the data, however, it's clear that in some cases the procedures produce benefit.

UNIDENTIFIED SPEAKER: Can I comment on that?

DR. YANG: Let me finish. Okay.

Dr. Richardson.

DR. RICHARDSON: As a surgeon, I consider the risk from being shocked and having a small burn on your arm pretty minimal. But the population that should be selected are the ones that respond. So a retrograde analysis of evaluation of patients and the ones who respond in

that subpopulation can be used to try to identify patients who are good candidates. But other than that, I don't know what else we could do.

DR. YANG: Thank you, Dr. Richardson.

Ms. Mattivi.

MS. MATTIVI: No. I think there's not enough data to really support attribution of this device to the results that have been presented.

DR. YANG: Dr. Reppas.

DR. REPPAS: John Reppas.

I would say yes, but the evidence base is weak. I would also echo the comments made previously that this is sort of unknowable, right? The appropriately controlled experiment, to really answer this question around efficacy, is almost impossible to design, certainly unethical to do. And there's no sponsor who is going to pay for it.

DR. YANG: All right, Dr. Park. Sorry, Dr. Kim.

DR. KIM: I think yes. And I just want to qualify that, however. And this echoes what Dr. Fost mentioned. I'm incredibly sympathetic with Dr. Dorsey's reservations about the evidence base. However, my reading of the evidence presented by FDA review shows that the evidence base for positive behavioral therapies, as well as drug therapies for the seriously self-injurious group, is fairly equivalent, as far as I can tell. Not only that, the evidence base of the side effects of the medications is very persuasive and rigorous, actually. And that's well established.

So I think that we need to be careful not to apply a particularly high standard in just the efficacy. I think it is a really important question of balancing the efficacy and risk. But in terms of efficacy, I just don't see -- unless you apply a special epistemology here, I just don't see why we would single it out as having different -- given the literature is pretty much similar type of data for the other alternatives.

DR. YANG: Thank you, Dr. Kim.

Dr. Stebbins.

DR. STEBBINS: Glenn Stebbins.

I would say, based on the testimony, we do have evidence of efficacy, be it as limited as it is, and from the testimony, some of the testimony, it appears that efficacy is for those patients who were refractory to other treatments.

DR. YANG: Dr. Peavy.

Thank you.

DR. PEAVY: Guerry Peavy.

I would give it a weak yes. I think that it probably does work for some people. I'm not able to characterize those at this point. It's the same issue as the specific subpopulations.

That's it.

DR. YANG: Thank you.

Dr. Augustine.

DR. AUGUSTINE: Erika Augustine.

I similarly think I have to give a weak yes. I'd really like to give a maybe, but I have to choose yes or no. I'll go with a weak yes. I think we are so limited by the quality of evidence that has been presented. It's not an overwhelming number of case reports; they're really a small number. We don't have a great sense of the denominator in the sense that we don't really know how many have been exposed to this therapy in order to even, on an open-label basis, really have a sense of a responder rate.

We have questions about some of the data with the 100% responder rate in one of the larger case series, and it's really hard to think of any intervention that really has a 100% rate. And so even with the limited data that we have, at least one of those series, I think there are questions about the validity of that data. And then comparing that 100% responder rate just to the variability and the testimony that we had today, again, further puts that into question. So it does seem that, based on these case series, there is a possibility that there's benefit, but it's very hard to know how much that differs from what a placebo rate would be. So potentially.

DR. YANG: Thank you, Dr. Augustine.

Dr. Connor.

DR. CONNOR: Jason Connor.

So I think there is weak evidence. You know, Dr. Dorsey said there's no RCT data, and that's all true, but it seems like the patients in whom

it's administered have exhausted all other avenues. And obviously this is not a light decision that parents make, and they make it after exhausting those other avenues. In particular, it's a last resort given the states that have banned such devices get waivers to send their students or patients there.

You know, Dr. Blenkush invited trials, but one of the reasons -- it was probably not evident. The reason I asked if judges ever said no to this is because that's a perfect control group. It's patients who they wanted to use this device on, whom they weren't allowed to use the device on, and I was going to suggest that FDA identify those patients and use that as a control group, which would have been interesting. But we can't do that since there were no such patients. But I think there is at least weak evidence that this works in some patients for whom nothing else has worked.

DR. YANG: Thank you.

Mr. Mikita.

MR. MIKITA: Yes. I say an unequivocal no. It's a firm no. It's a confident no. These are the most vulnerable people in our society. They lack capacity to consent; they cannot consider their treatment options. They have been muted and silenced for years, all their lives. Dr. Dorsey has it right. It is scant evidence, it is emotional evidence, it is anecdotal evidence. That is not evidence. That is not persuasive; it's not controlled. You can jump through as many kinds of rhetorical hoops as you can; it just doesn't carry the day. It's a harm; it's not a benefit.

DR. YANG: Thank you for your views, Mr. Mikita.

So Dr. Goodman.

DR. GOODMAN: I do believe, for some of the anecdotal evidence, that individual cases that are refractory are the treatments that were benefited by this treatment. But when I apply a higher scientific standard, I would have to say no. And the reason I would pick no rather than yes is that I would not want to see this treatment more broadly utilized across the country. You know, we've been talking about one center, but if you think in terms of what does our vote mean or opinion mean in terms of what kind of endorsement will that be for the rest of the country, I am certainly not ready to say that there is sufficient evidence to have this treatment disseminated. I would require more rigorous studies to be performed. And unfortunately, as was alluded to, that may be very difficult.

DR. YANG: Thank you.

Dr. Miles.

DR. MILES: I would say a firm no. The reviews date to 1966 to 1989. That means the data is more than 15 to 50 years old. I can't think of any other comparable risk therapy that is allowed to persist on such old data. None of that data pertains to the GED-3A or GED-4, which was modified after approval. The plural of anecdotes is not data, especially when it comes from a single treatment center with a conflict of interest and which is simultaneously applying multi-modal milieu therapy.

There are no subpopulations within the treatment facility for which selective efficacy exists. We don't have a denominator. The device has been modified. There's no way to dose the device for particular individuals to allow for daily sweat variation.

And, furthermore, the fact that the effects that have been seen in the older reviews were short-term rather than long-term suggest that the device does not cause learning, but rather it suppresses behavior by fear suppression rather than teaching learning. That makes this a restraint, not a treatment, and I strongly vote no.

DR. YANG: Thank you, Dr. Miles.

Dr. Bickel.

DR. BICKEL: Warren Bickel.

I'm not sure. I hear these case studies on both sides, and they're powerful, but I don't know. And the thing that I find most troubling is the absence of knowledge about the stimulus parameter space. That is huge, the parameters that can be varied there. We don't know a single thing. It's just that we have one parameter. I couldn't imagine, like, in a drug study, you'd just say well, the only thing we could think about is 40 mg of X, right? So I think I just don't know. But I think that there are enough recalcitrant cases that it would be good to know.

DR. YANG: Okay. So since five people have mentioned Dr. Dorsey's name around the Panel, it is only fair that although I want to

make sure that we address this question, not stray too far into future research studies and all that, it is relevant. And so I feel like it must be fair to have Dr. Dorsey do a short comment on the other comments that went along those lines.

DR. DORSEY: So medicine is full of examples where we thought intervention worked, but when we actually tested in a rigorous way, it didn't. One that comes to mind is using bone marrow transplants for the treatment of breast cancer; that was standard practice. There was no evidence, no high-quality evidence, for it. We did it, it didn't work. And not only didn't it work, it's a harmful procedure. There are simple ways that you can do prospective studies with independent raters. You can do a cohort study. We can even do randomized controlled trials for patients with refractory epilepsy, refractory to current treatments; we do that all the time. There's no reason, outside actual considerations which I share with my colleague, that that can't be done here.

DR. YANG: Thank you, Dr. Dorsey.

So, Dr. Peña, in answer to Question 2a, the Panel is split; essentially 60% and 40%, objectively. However, I must say that subjectively, the noes were very certainly no and the yeses were very weak yeses, to quote some of the Panel members.

And the concerns are that these are anecdotals or testimony; the quality of evidence is quite poor with very poor methodology in the

available studies.

There is some controversy, as you heard, among the Panel about the studies and whether or not we have the tools versus the ethical considerations. But this is a difficult population to study as this is obviously a population that is vulnerable, does not speak for itself, has not spoken for itself in a while.

As far as to trying to figure out what specific populations, I think unanimously around the table, the only suggestion was those patients refractory to other treatments. Other than that, it is very hard to define whether the subpopulations might have benefits.

Dr. Peña, is this adequate for an answer to Question 2a?

DR. PEÑA: Yes, thank you.

DR. YANG: Dr. Bowsher, 2b.

DR. BOWSHER: Question 2b: FDA has identified the following potential risks related to the use of ESDs that are intended to administer a noxious electrical stimulus for the treatment of SIB and aggressive behavior: other negative emotional reactions or behaviors, burns and other tissue damage, anxiety, acute stress/PTSD, fear and aversion/avoidance, pain/discomfort, depression (and possible suicidality), substitution of other negative behaviors (including aggression), psychosis, and neurological symptoms and injury. Please comment on whether this represents a complete list of risks, whether there are any additional risks that you think

should be included, and whether any of the risks listed above are not risks posed by ESDs.

DR. YANG: So the way I'd like to do this is first to again try to ask a yes/no question, whether this represents a complete list of risks. If the answer is no, then please state your addition to the list, or if there are any of the risks that are on the list that you think should come off the list.

So to be fair, I guess we should start with Dr. Bickel and go around to my right. So, Dr. Bickel, first of all, do you think that this list is complete?

DR. BICKEL: No. I think we talked briefly about equipment malfunction, and that should be on the list.

DR. YANG: Thank you.

Dr. Miles.

DR. MILES: No. I think that they should add mistrust or hatred of providers, learned helplessness when used as intended, trauma from falls, jerking body parts against furniture or the floor. And, finally, I would just point out parenthetically that I think the postmarketing surveillance of this device has been flawed by noncompliance with 21 C.F.R. 803.

DR. YANG: Thank you, Dr. Miles.

Dr. Goodman.

DR. GOODMAN: Yes, I agree that that list should be augmented by the adverse events mentioned by the previous two panelists.

DR. YANG: Mr. Mikita.

MR. MIKITA: I would say that the list is incomplete, and I would join Dr. Miles in noting some of the other risks. I think that some of the coupling bothers me because the way it reads, I think that if some of the -- you know, possible suicidality. I mean, I don't really -- that might be an FDA DSM-IV kind of thing, but I think that to really gain the weight and gravity and the harm and injury done to these individuals, that you've got to piece out each individual potential injury so that it carries the weight of what that person has been subjected to.

DR. YANG: Thank you.

Dr. Connor.

DR. CONNOR: I agree there are things that need to be added to the list that are discussed. I also think, from a trial and evidence perspective, some of these things may actually result from untreated disease or disability. So it's tough to tease out what is the disability and what is the device consequence, which is the reason we need blinded raters or much higher quality evidence to figure out what is the result of what.

DR. YANG: Thank you.

Dr. Augustine.

DR. AUGUSTINE: Erika Augustine.

I think the answer is no. I think there are some elements that are relatively vague, for which we really don't have much additional

information, thinking about the term "other tissue damage." When we think about electrical shock or electrical stimulus, most of our medical knowledge relates to a sudden large one-time kind of shock and not necessarily smaller amounts of lower current on a repeated basis potentially over years.

And to my knowledge, we don't have a good understanding of that and at no point in time over the last 40, 50 years has there been a systematic look at potential injury that relates to cardiac effects, renal effects, muscle damage, neurological symptoms like neuropathy, and all of which could be happening at low levels, and we don't know what the impacts on individuals who are exposed for a period of years to this therapy, what those might be down the line. So "other tissue damage" is something that I think we need to know a lot more about.

As it relates to pain and discomfort, again, based on testimony that we saw today, as well as video, I think understanding of the breadth and the range of pain experienced by individuals is really something that we don't know a whole lot about.

I also have concerns about the malfunctioning based on the data that was given of six inadvertent applications within 60 individuals in a year period; that's a malfunctioning of about 1%, which is pretty high. That's something that we really need to understand much better and to figure out how that can be addressed if this is to go forward.

And then I have other concerns that aren't exactly risks, but

probably won't come up in later questions, and first is do we necessarily understand what the right dose is in terms of what's the right dose to administer? We don't understand dose in terms of what is actually received by the patient as it relates to gender, ages, weight, body mass index -- you know, body fat, that sort of thing. We really don't understand the implications neuropsychiatrically for children that may differ from adults.

And then again I think we still have to go back to the concept of really thinking about the fact that this is a device largely intended for use in vulnerable populations. So a number of concerns.

DR. YANG: Thank you very much.

Dr. Peavy.

DR. PEAVY: Guerry Peavy.

I don't feel that the list is complete. I think another vague term is "neurological symptoms." I believe pretty strongly that some of the people suffer from chronic stress; hard to know how long that lasts, but we do know that chronic stress can affect certain parts of the brain and can affect cognition.

Another issue is poor sleep. And some of these may be a little bit subsumed under the others, but it's probably an advantage to try to be a little more specific. So even just poor sleep could also lead to cognitive problems, attention, concentration, learning.

DR. YANG: Thank you.

Dr. Stebbins.

DR. STEBBINS: Glenn Stebbins.

I would say no. I agree with the comment about pain should be added since it's an obvious one. Also, the stimulus generalization. We had a couple of testimonies where patients said that if they heard Velcro, they would suddenly react to that, so I think that needs to be on there.

And then I think the term "psychosis" is a little bit vague. I'm not sure that I really heard that in any of the testimony or read that in any of the documentation.

DR. YANG: Thank you.

Dr. Kim.

DR. KIM: I agree with the previous comments. To think about risks, we want to err on the side of being overly sensitive so we don't miss anything. And I think that I agree with many of the comments that have been made previously.

DR. YANG: Thank you.

Dr. Reppas.

DR. REPPAS: I think that list, inconclusive of my colleagues' comments, is fairly comprehensive, so I would say yes. I would also add, though, that just as the character of the efficacy evidence is undermined by its anecdotal nature, the same concern applies here particularly when many of these things, as we all know, are co-morbidities with the group of people

that we're thinking about. So in the same way that we need to have a high standard about efficacy, we should have a high standard about risk. That being said, this is a fair list.

DR. YANG: Dr. Reppas, just to clarify so I don't misspeak on your behalf, you are saying yes if we include all those other things?

DR. REPPAS: I would say yes, the list is inclusive, but I also am seconding my colleagues' comments in aggregate that those other things ought to be added.

DR. YANG: Okay.

All right, Ms. Mattivi.

MS. MATTIVI: No, I don't think the list adequately describes the risks associated with this. Again, we're dealing with a vulnerable population. To be spending years in an environment that is controlling and under these kinds of circumstances, I don't feel that the list adequately represents potential long-term emotional sequelae from living in this kind of environment.

DR. YANG: Thank you, Ms. Mattivi.

Dr. Richardson.

DR. RICHARDSON: No, I don't think it describes possible side effects. We've already heard about peripheral nerve injury and some other things. All the way, this is a perfect paradigm for the learned helpless, this syndrome, producing pain in people who have no control over the pain.

There is a huge number of studies that were done after World War II on the learned helplessness paradigm, and in fact, it's still being used by drug companies because it produces in animals something analogous to depression and it can be used to test antidepressants.

So I'm surprised that they haven't reported -- and maybe there is -- I haven't noticed that they reported any severe depression. So obviously the research is poor. The only people using the device have not reported their results, side effects, complications well. And obviously we need a better device. I mean, there's no question about that.

DR. YANG: Thank you.

Dr. Iwata.

DR. IWATA: No. I agree with risks other people have identified. I'm not sure if you were talking about this phenomenon, you spoke about learned helplessness. There's another phenomenon in the punishment literature known as generalized behavioral suppression. That is when experiencing a great deal of punishment, some people just stop behaving in general. Adopted behavior drops off also.

DR. YANG: Thank you.

Dr. Green.

DR. GREEN: My only addition, beyond what other people have said, is amplification of the pain because there are plenty of models in medicine that when you have repetitive bouts of peripheral pain, a

percentage of people go on to develop central pain or phlegmatic pain, which then has a life of its own, and people often report allodynia, for example, and if they develop allodynia further, impulses of pain are further amplified. Ask 10 people who have had shingles, and they'll tell you about this syndrome.

DR. YANG: Thank you.

Dr. Weigle.

DR. WEIGLE: No, this list is not complete. I agree with everybody, what they've added. And I think that Dr. Peavy kind of brought up the cognitive effects and impairments, particularly over the long term. That needs to be tracked closely for people who are already neurologically compromised.

And one thing -- I can't say it's a direct effect of maybe this device, but it may be an effect of using this device, an effect on treaters in that they may not -- what could occur and probably does occur, at least some of the time, is that other conditions and problems are overlooked because everything that occurs will be attributed to this treatment rather than perhaps -- and I guess there was one example, a broken tooth that was overlooked.

And we know that a lot of people in this population for whom this is being used also have a lot of medical complications as well as psychiatric conditions that are very often unrecognized. And the number one symptom of psychiatric problems for this population is aggression in some

form. So I fear other causes are overlooked and untreated.

DR. YANG: Thank you, Dr. Weigle.

Dr. Fost.

DR. FOST: Norm Fost.

I have five brief comments.

One: I think the list, as supplemented by colleagues, is adequate. I mean, it deserves to be supplemented.

Second: Picking up on Dr. Richardson's comment from 20 minutes ago, these risks are modest compared to many, many other things we do. And when you give chemotherapy, we don't say, oh my god, but look at the risks; we can't possibly be giving toxic drugs like that to people. You do it because they're desperate. This is about as horrendous a condition, a psych/behavioral condition, as I can think of. This is just the bottom of the pit. So these are desperate patients suffering enormously, psychologically, and physically. Incapacitated, restrained, isolated. So it seems to me it's appropriate to look for therapies that might have very substantial risks, such as we do for other diseases. These risks are pretty modest, as Dr. Richardson said. Compared to surgery, this is not much.

Third point: A comment about learned helplessness with respect to my distinguished colleagues who have made comments on it. This is not about learned helplessness. Learned helplessness is about non-contingent pain. The essence of it is pain that you can predict when it's

coming because whether you're doing it in rats or in prisoners of war -- because it has no antecedent that comes out of the blue.

The whole idea of this kind of intervention is that it's very predictable, that it happens when you behave in a certain way, and that the patient learns that -- if it works, he or she learns that very quickly and that makes them not be subject to this pain. So whether that actually works with it, there's benefit. We all agree we need better studies. But this is not about learned helplessness.

Finally, because it only fits here, I just wanted to say something about the word "torture," which has been used about a hundred times today. My friend, Steve Miles, is the world's leading expert on torture, so I'm humble about commenting on this in his presence. Torture, in its familiar term, is about state-sponsored physical harm and suffering inflicted on people to obtain information for the benefit -- or to change their behavior for the benefit of the state. Or it's about psychopaths who do this for pleasure. The essence of it is it's not done for the benefit of the person being tortured; it's done for somebody else's benefit or interest or craziness.

If this is torture, then my neurosurgeon who did brain surgery on me was committing torture. It was pain considerably worse than what we're describing here. But I don't think he should be accused of torture. He inflicted horrific pain on me for a reason, to help me with a problem I had, namely, a brain tumor. These people have a terrible problem and inflicting

pain on them, if it helps -- if it helps their problem go away, then it's just as appropriate as brain surgery was in my case. Torture is not the word for these kinds of clinical interventions.

DR. YANG: Thank you.

Dr. Dorsey.

DR. DORSEY: So I agree with the other panelists about what should be added. The difference, though, on this pain issue, that the neurosurgeon took steps to mitigate the pain that was delivered -- actively took steps to mitigate the pain that was delivered. In this case, the whole purpose of the intervention is to cause pain. Moreover, the neurosurgeon is a health professional who had 10 to 20 years of training in the care of patients. Here we have people who aren't health professionals who are administering this treatment.

That is greatly concerning. It's greatly concerning to me that the first warning on page 1 of the user manual -- that we haven't been updated on -- is not followed. The fact that individuals who are not licensed professionals are carrying out this is a visceral disgust, I think, that strikes in a lot of us, that people who aren't adequately trained are given the power to inflict pain on others. The first principle of medicine is do no harm. That's clearly being violated here.

DR. YANG: Thank you, Dr. Dorsey.

All right, Dr. Armstrong.

DR. ARMSTRONG: Daniel Armstrong.

I had put down some comments that I'll save for 3, but there are -- I would say no to this question. And there are three points that I think we have not completely mentioned.

One: To follow up on Dr. Weigle's component, the impact on staff. You know, one of the things that you learn in Psych 101 is the Milgram experiment. And we learned that after a period of time, individuals who are in the position to inflect pain will change their tolerance for that infliction of pain. We also know that from a number of pain studies, that pain behavior and disruptive behavior is aversive to the individuals who are there. And it's very simple to shift from the recognition of the behavior to an attribution to the person. And those are risks that occur in this environment in a significant way.

I would disagree somewhat with Dr. Fost because we have heard today, at multiple points, that because of malfunctions and because of inappropriate -- potential inappropriate -- use by untrained staff, there is non-contingent application of this device. And in a perfect world where the behaviors were clearly defined and everything was contingent, that wouldn't be an issue, but we've heard clearly that there are multiple episodes of non-contingent infliction, including malfunction of the device.

The third, and I think one of the most important components about this risk issue, is that the concerns that are addressed most

passionately about the risks to individuals in terms of respect, depression, anxiety, stress, those are risks that we measure in the rest of the population by self-report, and we do not have the capacity in a number of these individuals -- they don't have the capacity to self-report accurately on what's going on. So we really don't know what those risks are. We can only make determinations by an expert or someone from the outside looking at the behavior and making an interpretation. And we know how poorly that works in other populations.

DR. YANG: Thank you, Dr. Armstrong.

Since learned helplessness apparently has been mentioned, I believe, four times around the table, I'm going to pass this back to Dr. Miles for a short comment about learned helplessness.

DR. MILES: Norm got me into this field, so I'm going to be brief. I do think that this is appropriate, to consider learned helplessness, because these people have learning disabilities, and if they don't recognize the stimulus for which this thing is being applied because of their learning disabilities, then they can't learn and it's not contingent behavior. That is entirely even apart from the question of the device malfunctions.

If a woman doesn't understand that lifting her arm to hear is part of the head banging problem, then there's going to be a serious problem in terms of how she's going to respond to an environment that bangs her when she reaches out her hand to shake hands with somebody.

DR. YANG: Since this is not about learned helplessness, let me just cut it there.

So, Dr. Peña, with regard to Question 2b, it is the feeling of the Panel that no, this is not a complete list. Now, you heard that this is a very long set of comments, so let me try to group this into sections.

First statement I'll make is that this is a very vulnerable and very complex population that does not seem to be able to self-report, so therefore the point has been made that we need to be more sensitive to these risks than less.

The second point that I should make is that these terms that are listed here may be too vague, that they need to be more specific. And there are some specifics that I'll put under that as part of my first point.

Now, the first is equipment malfunction, pain, long-term effects and range of pain, amplification of pain, trauma from falls.

Then comes a class of mistrust of providers, question of learned helplessness, generalized behavioral suppression.

Also, there is a question of smaller repetitive damage as far as other tissue damage goes.

Then cognitive neuropathies were mentioned several times. Neuropsychiatric symptoms and emotional sequelae.

Point No. 2, though, is that there is some controversy about the modesty or the severity of these risks, especially compared to the brutality of

the disorder, itself.

And then lastly, the effect on staff, I think, is very important. The one is upon the staff, themselves, and their tolerance for it, as well as their masking other problems in these patients for them.

So the answer is still no, and I tried my best to add to the list there. Dr. Peña, is that adequate for Question 2b?

DR. PEÑA: Yes. I would also like to acknowledge that revising this transition, how we might consider all the available information. And all that you have heard from all stakeholders in the overall push for this class of devices is appreciated.

DR. YANG: Thank you, Dr. Peña.

Dr. Bowsher. For Question 3.

DR. BOWSHER: Question No. 3: Section 516 of the Food, Drug, and Cosmetic Act (21 U.S.C. § 360f) sets forth the standard for banning devices. Under that provision, FDA is authorized to ban a device if the device presents "an unreasonable and substantial risk of illness or injury" based on all available data and information. Considering the adequacy and availability of alternatives to treat patients exhibiting SIB and aggressive behavior, as well as the benefits ESDs may provide for these patients, please discuss whether ESDs intended to administer a noxious electrical stimulus for the treatment of SIB and aggressive behavior present a substantial and unreasonable risk of illness or injury. In your response, please explain your

reasoning.

DR. YANG: So to restate, the question here is does the available evidence show that this presents a substantial and unreasonable risk of illness or injury? I realize that this is obviously a difficult question to answer, but we're going to try to ask you for an affirmative or a denial. Also, depending on which way you vote -- or sorry, not vote. Depending on which answer you give, if you could please explain the reasoning behind it.

So, again, to be fair, I think this time we'll start in the middle. So could we start with Dr. Fost and then head around?

DR. FOST: Norm Fost.

Whether the risks are commensurate with the benefits and therefore whether they're reasonable or unreasonable depends on better information. I think there's plausible reason to think they might be, but I think we all agree that the evidence is weak and that it would be much better if we had well-designed studies. If those studies show that there's really tremendous benefits, then the risks might be commensurate, just like for other horrendous conditions. So we don't know, but I think it's plausible that the risks are reasonable if there turns out to be benefit.

DR. YANG: Okay.

Let's see here. Dr. Dorsey.

DR. DORSEY: So I'll break it into two parts. The first question, is there a substantial risk? And the second, is there an unreasonable risk?

And so for the substantial risk, the question, to me, is like what is the likelihood of harm, of injury? And I think, here, unlike the vast majority of things that we prescribe or devices or treatments, the likelihood of injury or illness is virtually 100% if the device is functioning as it should. So I think there is a substantial risk of illness or injury from the device.

Then the question, is this unreasonable? So you could imagine extreme cases whereby you might engage in an intervention that causes harm to prevent greater harm from occurring. So, for example, head banging. If you could prevent head banging with an intervention that caused harm, you might say that would be worth it for the benefit. Here we have the case of uncertain benefits and we have certain risks. And these risks are probably in the mild to moderate range. If you look at the ratio of risk to benefit, you have certain risks and uncertain benefits, and for that reason I think that you both have substantial and unreasonable risk of illness and injury associated with these devices.

DR. YANG: Dr. Dorsey, thank you.

I am glad that you brought it back together because obviously, if I want to restate this question, this is a question about banning devices, and as it is stated here under that provision, FDA is authorized to ban a device if it presents an unreasonable and substantial risk of injury or illness. So I'm going to ask the Panel members to consider that as one for this purpose.

DR. PEÑA: And, Dr. Yang, I would just -- if it's helpful to the

Panel, they should evaluate the data that they have available, not what might be.

DR. YANG: Thank you, Dr. Peña, for that.

Let's see. Dr. Armstrong.

DR. ARMSTRONG: Daniel Armstrong.

I agree. I think that this represents an unreasonable and substantial risk of illness and injury. And the data that we have suggests that for some individuals, the risk is there and is both substantial and may be unreasonable. And I think the basis for that consideration, my mind is that we've not had the discussion today, but there is substantial literature on individual variation in pain perception and pain tolerance. And this is a one-size-fits-all application without any assessment of that particular issue. And that, for me, is a hugely influencing factor in that decision.

There are also, in this process -- I've not heard any discussion of evaluation of individual responses and stopping points if there is either no response nor an adverse response. What I have heard is that if there is no response, we intensify, which is concerning.

A third component that is here that is related specifically to the device -- and I think one of the challenges that I struggle with and perhaps we struggle with -- has been the separation between the device and the way that it has been used in this one institution. And those really are inseparable, but they are still significant concerns. But there are problems with the device.

The rate of malfunction is a real concern, and it's a concern not only for people being non-contingently exposed to a painful and aversive event, but it's also -- from the clinical perspective of the application and operant paradigm, to have an operant paradigm that throws in non-contingent shock really sort of throws the whole paradigm out the window, depending on its occurrence. And so I think there's a real problem with the device that makes me answer the way I do.

DR. YANG: Thank you, Dr. Armstrong.

Dr. Bickel.

DR. BICKEL: Warren Bickel.

I don't think we know enough because, as we talked about before, some of the potential negative downsides may be secondary to the disorders that they present and -- this is a cost-benefit analysis, right? And we have to look at the cost and the benefits. And if we don't exactly know what the costs are and we don't exactly know what the benefits are, I think it's going to be very challenging.

I think it's a tremendously important point that was raised just before, that we separate the class of devices from the institution and this particular device. And this particular device is challenging because of malfunctions and perhaps some of the procedures that are used in this particular application are challenging.

The question is, is there benefit for recalcitrant self-injury

where people are gouging out their eyes and doing bodily harm to themselves, to think about some procedure that could help them? I don't know. But I feel, for those recalcitrant traces, that we should try to get knowledge to --

DR. YANG: Thank you.

Again, I just want to restate the actual question because of the circumstances that we are in. So we are asking you to consider unreasonable and substantial risk of illness and injury as one category. I understand the limitations. I, myself, have trouble with this. But to the extent that you can, if you would please address that rather than benefits or otherwise.

DR. MILES: Steve Miles. I'll do my best.

Yes, I think that the risks are unreasonable and substantial. And there is a problem here in the question of -- revoking the exemption is different from the question of banning.

But, first, I think that the statements of professional programs and the fact of wholesale abandonment of aversive electrical shock therapy by the peers in this field show that it is unreasonable to conclude that these devices are part of the standard of care for this class of patients, and that therefore that suggests the device should be abandoned.

Secondly, I think that the FDA exemption may unreasonably mislead patients' guardian ad litems in the courts who supervise these decisions as to the efficacy or safety of these devices, which is a finding that

is currently without foundation.

Third, given the lack of data on efficacy and the very tangible adverse effects, I think that the risk to benefit clinical ratio, leaving out cost effectiveness, is negative, and I think that this device is counter-therapeutic to the patient population for whom it's intended because of the issue that many of them with learning disabilities cannot evaluate the nature of the stimulus.

And so I would say it's unreasonable, it's substantial, and that that implies that the exemption should also be discontinued entirely apart from the banning question.

DR. YANG: Thank you, Dr. Miles.

Next we have Dr. Goodman. I also wanted to say that these are all very important points, so please keep your statements as concise as possible so we can get around, as we've got time limits.

DR. GOODMAN: Sure.

I believe that the criteria of unreasonable and substantial risk of illness or injury for the banning criteria are met in this case. And like other panelists have mentioned, it's very hard to disentangle that opinion from the assessment of benefit, which is very weak. And so I might have come to a different conclusion if I felt that there was a wealth of data supporting its efficacy given the extreme harm that could come to these patients; examples that we've heard of people nucleating themselves or retinal detachment.

These are very serious problems.

So that said, I believe the criteria are met. The only concern I have -- and I know we've been warned on this -- is certainly for the class of available devices, I would ban them, but I wouldn't want to foreclose on a future generation of more sophisticated devices where maybe the noxious level could be adjusted or individualized. One could conceive of not just pain, but some sort of distracting stimulus that might serve a similar purpose rather than pain. So I would consider in the future -- I hope there would be consideration for more sophisticated, safer, and less noxious devices that might serve the same purpose.

DR. YANG: Thank you.

Mr. Mikita.

MR. MIKITA: I would say, as Dr. Goodman has just said, that the term "an unreasonable and substantial risk of illness or injury" has been met, and it's been met with data and testimony, and you have to kind of step back and just work at this case very, very simply. And it's about one place in this country that uses a device on the most vulnerable people in this country who cannot give consent. And if you do not have a visceral reaction after today, then you don't have a visceral reaction to anything.

DR. YANG: Thank you. Again, we are considering the class of devices, not one institution, just to make that point.

Dr. Connor.

DR. CONNOR: Jason Connor.

So I think I lean a bit with Dr. Fost in that there are lots of devices and procedures and drugs that have very clear adverse event profiles that are far, potentially more damaging than this that we allow in case-by-case basis to weigh benefits and risks. It's a tricky question because it seems like we're being asked about a class, but we're hearing about one particular thing. And so my concern is that I wouldn't want to ban the class because I would ask if there are cases under direct observational supervision, you know, when a patient is only about to harm him or herself, not doing some of these what seem like small things where they're getting punished, not prohibited from causing harm.

You know, if there's a clear protocol where if a patient isn't responding within the first few days and learning, we stop, because the mental disability is prohibiting learning from happening. We heard from a few very, very eloquent patients who have used this device and thought that it led them to go back into the real world -- that's probably a bad term but, you know, to be part of the community. So could it be labeled for "only for verbal patients" and only for patients who can discuss adverse events immediately after administration of the therapy?

So I think one of the big questions before a ban can happen is, are there ways to change the label? So given this is even in the future of other potential devices, I think there are many ways to construct a label that

protects the most vulnerable patients and also allows for the potential to help patients for whom every other therapy may --

DR. YANG: I'm going to stop you there because the labeling is our next one. All right.

So you're all impressing me with your eloquence. So let's go for concise.

All right, Dr. Augustine.

DR. AUGUSTINE: Erika Augustine.

I think we have insufficient data and information available to answer the question. We all agree that there are a subgroup of patients who are inadequately treated for what are very severe life-threatening, life-changing behaviors. The overall degree of benefit, if there is benefit, is unclear. The frequency of adverse events, we don't know. The severity of events that occur and the range of that severity, we don't really know. So it's very difficult to say whether or not some of the isolated factors that we've heard about are unreasonable with respect to the potential injury which can be quite severe.

We've talked about vision loss. We haven't talked about intracranial hemorrhage that has happened with head banging in select patients. So these are extremely severe disorders, but we really don't have sufficient data to answer the question.

And I think one thing that we haven't talked about is the social

context and whether or not these are socially acceptable treatments, as well, which is a little bit different than risk. But we have 40 states and a United Nations who have advocated for banning of these devices, and again, it's very hard to disentangle that, but I would say in summary, we have insufficient data to answer the question.

DR. YANG: Thank you.

Dr. Peavy.

DR. PEAVY: I would say yes to the question, and I think that the main reason for that is because we are not able to individualize or put people in subgroups because of a lack of information.

DR. YANG: Thank you.

Dr. Stebbins.

DR. STEBBINS: Glenn Stebbins.

Yes, I agree that there is evidence of excessive and -- sorry. Substantial and unreasonable risk. And really I base this on what Dr. Dorsey said, and I think it's true, that the risks are clearly present and the benefits just are not known.

DR. YANG: Thank you.

Dr. Kim.

DR. KIM: Since I'm going to be one of the minority, I hope you'll indulge me for just a few seconds.

I concur with Dr. Fost and Dr. Connor on this issue. I think that

we seem to be applying a special standard for this situation, and I think that is probably because one of the issues that Dr. Dorsey very eloquently brought out, which is that this treatment involves causing direct pain, and that is extremely troubling. And I think that for those for whom that causes an incredible visceral reaction, this will never be an acceptable therapy, and that really reaction has nothing to do with risk and benefit calculation, in my mind, unless you, by definition, bill that as substantial harm.

And I respect people who have that view because I think that's a reasonable, morally sensitive perspective. I do think, though, other people who are also morally sensitive might not share that, and if you exclude that and try to do a risk/benefit balance for the families and patients in the kind of situations that we heard about and what we read about -- I mean, sure, they're anecdotes, but there are 32 cases that I read of multiple pages' description, as well as the fact that the case reports aren't case reports like we do in medicine. These are individualized experimental protocols, which are actually a little bit different because they -- although they're not really perfect, they do get at the cause of mechanism somewhat more so.

Just one more second. If we apply the standard to the antipsychotics, for example, we should be banning the antipsychotics because there is convincing evidence that you could say -- I honestly don't know if really, on the aggregate, it really justifies use if we use the current standard for banning this. So I would really say that it depends on the standard we

use, and we should understand why we're saying it.

DR. YANG: Thank you, Dr. Kim.

Dr. Reppas.

DR. REPPAS: John Reppas.

I think this is an extraordinarily difficult decision, but I do not agree with this assertion, and the reason for that is that I don't think that the often poor behavior of this particular sponsor -- I think the sponsor has fallen short of their obligation in many, many ways -- should not, nevertheless, jeopardize the category, the therapeutic category, and I think that there is potential for future innovation around this therapeutic premise that can be much more effective, much more compassionate, and can really address a need effectively in ways that the existing therapies don't. So I'm very reluctant to say yes to this.

DR. YANG: Thank you.

Ms. Mattivi.

MS. MATTIVI: Incredibly complicated idea, an incredibly complicated topic. It's an extremely vulnerable population that reminds me very much of the conversation going on at CMS right now around the management and controlling behaviors for demented nursing home residents, you know, and we're not shocking them. We're talking there about restraint-free environments and polypharmacy and management of polypharmacy.

I think a big difference in this is the human component that is not controlled for at this point in time, both from the people in charge of the application as well as the people receiving the shock. There is so much that isn't known about the dosage, how the machine is delivering the dose, how the body is receiving that dose, what is the individual person's pain threshold; there has been no assessment of that. There's no documentation of assessment of adverse events; they're a nonverbal population, for the most part.

There are just an incredible number of unknowns in this, and so for all of those reasons, as things stand with the data we've been presented today, I would say yes, there is an unreasonable risk of illness and injury. But also not wanting to preclude that future advances and future innovations in technology may provide some benefit.

DR. YANG: Dr. Richardson.

Thank you.

DR. RICHARDSON: Well said. My thinking is the severity of disease versus the risk of the procedure, and the severity of the disease is very severe. So that's one issue.

The other issue is that patients with Tourette syndrome and self-injurious behavior who, by and large, are much brighter than the average population on our measurements will opt for an operative procedure much more severe than this to try to stop their self-injurious behavior. And that

has been demonstrated many times. That's one of our criteria for operating on them, is self-injurious behavior.

In addition to this, our knowledge about violence and aggressive behavior is becoming more obvious. The use of functional MRI and PET scanning, et cetera, has made some very large progress in that area. And I think that this problem will be moot in about two years. But that's not our issue today, unfortunately.

DR. YANG: No.

DR. RICHARDSON: So, anyway, I'll leave it at that, but --

DR. YANG: Thank you.

DR. RICHARDSON: -- I have a publication in press that --

DR. YANG: Thank you.

DR. RICHARDSON: -- will address some of that.

DR. YANG: Dr. Iwata.

DR. IWATA: My problem is separating the class from the device and the device from where it's being manufactured and used. My understanding is FDA is basically focusing on the class and not on a device or where it's being used. And if one examines electrical stimulation, I can imagine an electrical stimulus that is not painful; it might be annoying. So, for example, you walk across the carpet, you put your finger on the stereo, that is an electrical stimulation. That's annoying. It's annoying enough for me to not want to do that again. And that deters a lot of my behavior.

On the other hand, we've got the GED-4, which I have not experienced and I hope I never do. If we were to look at other classes of devices such as, for example, visual stimulation, one would ask is it harmful to shine a laser in someone's eyes to deter them from engaging in behavior, and I'm sure everyone would agree, yes. But then what would happen if we ask, well, what if we shined a flashlight in their eye briefly? I'm not so sure about that. So I think it's entirely dependent upon the parameters of the class of devices, and I can envision parameters that really would not be viewed as noxious or painful by many people. So speaking about the class, I would have to say no.

DR. YANG: Thank you.

Dr. Green.

DR. GREEN: Well, I'm not sure, again, what the class means because clearly we need a very customizable device which then might be acceptable under various circumstances. I would say yes to a ban of the existing devices and somehow, by some other mechanism, encourage the development of others.

DR. YANG: Thank you.

Dr. Weigle.

DR. WEIGLE: Karen Weigle.

I agree with Dr. Green for exactly the same reasons. Yes to this device, but maybe there are other means of developing another device.

DR. YANG: Okay, thank you.

So, Dr. Peña, in answer to Question 3, 60% say yes, that there is an unreasonable and substantial risk of illness and injury, and 40% say no -- and I'm going to lump this in there together -- no or not enough data. It's hard to separate those apart.

The comments are -- there are many, but again I'll try to summarize -- that in the context of a weak and unclear benefit in a vulnerable population with a terrible disorder, that first of all, separating the class from a singular device and institution is very difficult to do. It seems like there is a one-size-fits-all device right now that cannot be individualized, and potentially this pain and this treatment for some individuals is very substantial and unreasonable but not so in others.

With regard to the device, there are no stopping points. We don't know what the noxious levels are. There has not been any investigation into the parameters. Again, there's just a single device.

And then, lastly, that although in this situation and this device, with the evidence presented today, that although -- you know, 60% majority, weak majority, says yes, that it's unreasonable, it should not preclude any other potential future development of devices like this one.

Is that adequate, Dr. Peña?

DR. PEÑA: Yes, with one comment, that legally, studies within an IDE, which is a way to study medical devices, are outside the scope of a

ban, though it may be difficult to obtain IDE approval for such a study.

DR. YANG: Thank you very much.

Okay, Dr. Bowsher.

DR. PEÑA: So, to clarify, that means that you could study a banned device under an IDE, though it might be difficult to obtain approval for the conduct of an IDE study.

UNIDENTIFIED SPEAKER: That's what I thought. I heard you say that, and I wanted to know what that means.

DR. PEÑA: So that would further mean that in the absence of a study before us all for discussion, you would need to have some review of that study, how it's designed, whether to approve or not, that IDE study. Do not preclude future innovation.

DR. BOWSHER: Okay, Question No. 4: If FDA determines that a device does present an unreasonable and substantial risk of illness or injury, the Agency next considers whether this risk may be corrected or eliminated by labeling, and they also consider whether imposing other requirements could correct or eliminate this risk. Please identify potential risk mitigations and discuss how they would address identified risks.

Examples of potential risk mitigation include but are not limited to:

- Restriction on device technology and use (e.g., electrical stimulation output parameters, limitations of number and/or

locations of electrodes permitted on an individual).

- Labeling restrictions [e.g., indication only for use in treating only certain populations (e.g., treatment refractory patient populations, patients in certain age groups) or indication for use only when significant injury is being exhibited (e.g., life-threatening injuries)].

DR. YANG: Okay. So what I'd like to do with this question is there were 10 people on the Panel that stated that it did present an unreasonable and substantial risk of illness or injury. I would like to go to those folks first with regard to this question about whether it can be mitigated, the risk can be mitigated, by labeling. Then I'll take just general comments from all the rest of you that said no or no data. So you'll have to remind me. I do remember that Dr. Fost said no, no data. Dr. Dorsey said yes. So do you believe that the risk can be mitigated by labeling?

DR. DORSEY: I would say that there would be no labeling changes that would prevent it from being a substantial and unreasonable risk. That said, I think there could be things that could be done to reduce its risk; chiefly, making sure that it's done by licensed health professionals. I would want the label to be restricted to people with self-injurious behavior, perhaps as documented by having injuries that required medical attention.

Those would be two off the top.

DR. YANG: Okay, thank you.

Dr. Armstrong, please remind me. Did you vote yes on the last question?

DR. ARMSTRONG: I did vote yes.

DR. YANG: Okay.

DR. ARMSTRONG: Actually, I'm not sure that there is anything that could be changed related to labeling at this point that would take care of the problems we have.

DR. YANG: Okay.

DR. ARMSTRONG: The one possible thing would be a limitation to those individuals who are engaged in behavior that is life-threatening or involves significant potential loss of an organ or damage to an organ of themselves or another. I'm concerned about the lower level of self-injurious and aggressive behavior.

DR. YANG: Thank you, Dr. Armstrong.

Let's see here. Dr. Miles, I believe, is the next one that voted yes.

DR. MILES: This is a non-validated technology. I don't think that mitigation can be discussed at this time. Question 6 addresses a research agenda.

DR. YANG: All right.

DR. GOODMAN: I can't think of a sufficient mitigation strategy using the existing devices. And if you think about titrating the level of

noxious stimuli, it's not clear that one can do that. It would be hard to calibrate, even within the same patient, over different time points. So I can't see a strategy that would be workable.

DR. YANG: Thank you, Dr. Goodman.

Mr. Mikita, you voted yes, as well.

MR. MIKITA: No feasible strategy.

DR. YANG: Okay, thank you.

I think you did not, and you did not.

And Dr. Peavy.

DR. PEAVY: I actually believe that labeling would be helpful if we knew what to put on the label, but we don't.

(Laughter.)

DR. YANG: Okay. So I'm going to take that as -- Dr. Stebbins, okay.

DR. STEBBINS: I voted yes. Glenn Stebbins. I stated yes.

Yes, I think that given the current device, there's nothing really to --

DR. YANG: Okay, very good.

Dr. Kim, please remind me. Did you vote -- you said no data, right?

UNIDENTIFIED SPEAKER: He said no.

DR. YANG: He said no, okay.

Dr. Reppas, you also said no.

Ms. Mattivi had a tentative yes, hopefully.

MS. MATTIVI: I think I agree with Dr. Peavy, that --

DR. YANG: Okay.

MS. MATTIVI: -- if we knew what to put on the labeling, if we knew that the people using the device were going to read and follow the label, that would be different.

DR. YANG: Okay.

Dr. Richardson said no.

DR. RICHARDSON: I'd just like to say that you can build a device that is programmable and can be -- you can measure patients' pain response. We've done that hundreds of times.

DR. YANG: Okay.

DR. RICHARDSON: And you can set a device that's uncomfortable but not panic stricken when they use it. This device has two levels. One is aggravating and the other is panic, and there are levels in between that can be used. And it's fairly easy to do. We did this years ago. And you could have a device that you could set for each patient.

DR. YANG: Can I ask you to reserve these comments for the potential research part? There's one --

DR. RICHARDSON: Right.

DR. YANG: -- coming up, okay?

Let's see. Dr. Iwata said no.

Dr. Green, you said yes, tentative.

DR. GREEN: Well, the problem isn't -- my objection isn't with the labeling. So no change is appropriate.

DR. YANG: No changes, okay.

And then I can't remember. I'm sorry, Dr. Weigle. You said yes?

DR. WEIGLE: I said yes to the last question.

DR. YANG: Okay.

DR. WEIGLE: So no, I don't think there is anything that we can mitigate.

DR. YANG: Very good, okay.

So, Dr. Peña, in answer to Question 4 about potential risk mitigation with labeling, 9 out of 10 said no, that no changes could mitigate this risk. If there were any comments, we're talking about things like we don't know what to put on the label, but you can't limit who's going to use it, but it would help if it was licensed health professionals, documentation of sequelae. And certainly limiting those to SIBs and aggressive behavior that has significant morbidity.

So, Dr. Peña, is that adequate?

DR. PEÑA: Yes, thank you.

DR. YANG: Okay.

Dr. Bowsher, Question 5.

DR. BOWSHER: Question No. 5: If FDA determines that a device presents a substantial and unreasonable risk of illness or injury and proposes to ban it, the Agency must specify whether the ban applies only prospectively or also applies to devices in distribution and/or in use by patients. Please discuss the risks and benefits of applying the ban to devices currently in use by patients and any recommendations regarding how patients should be transitioned to alternative treatments.

DR. YANG: So this can potentially be a very long question, but again, here there is a yes/no question in this, and that is whether or not the ban applies starting now or whether or not the ban applies to everybody that's using it before. So, please, if you can answer that question first, it would help. This is an important question that we should get everybody on the Panel's advice for this. Again, I ask you, please limit your comments to concise comments, please.

All right, how about Dr. Augustine? Let's start with you and go around.

DR. AUGUSTINE: Start with the question. If there is a ban, it should be applied to all of the devices in distribution. It's not so much that I'm advocating for a ban, but the risk of the device is either unreasonable or it's not, and there shouldn't necessarily be something special about the folks who are currently using it in terms of their risk/benefit and whether this is

reasonable or it's not. So it doesn't make sense, otherwise, in terms of the ruling, so I would advocate for all or none.

DR. YANG: Can you make an offer as to how you would transition someone?

DR. AUGUSTINE: Not necessarily advocating for the ban, but I think the transitioning is really a challenge because that's how they got to the device in the first place, is that they had exhausted other treatment options, and now you would imagine that those who are on it currently, there is some perception of benefit or it's been very early in their trial such that it's not clear as of yet. But for those where it seems that there has been benefit, I think it's going to have to be a complex set of discussions with their whole provider team and parents in terms of either revisiting old strategies or trying to think if they've absolutely exhausted everything.

DR. YANG: Thank you. I know, that's a very difficult question. I'm sorry to put you on the spot first.

Dr. Peavy, let's go with you next, if you could answer the question first. All devices or just those to come?

DR. PEAVY: I think Dr. Augustine's logic is spot on, so I think it would probably have to be all devices at the same time. You know, it breaks your heart to see people that have put all their hope in this working because they feel that nothing else has. Although for some people, it might be the best thing that would happen to them to take them off of this and try

something different.

DR. YANG: Okay.

Any comments on the transitioning or shall we leave it as "need a team of providers and very complex situation"?

Okay, very good.

All right, Dr. Stebbins. All devices or just those for the future?

DR. STEBBINS: Glenn Stebbins.

So that actually isn't the question, though. It's risks and benefits. That's what they want. But given the question that you're asking, I would say all devices.

DR. YANG: Okay.

DR. STEBBINS: And as far as transitioning goes, I think it's been said.

DR. YANG: The risks and benefits, I think, have been dealt with numerous times going around, so I'm going to skip that for now.

All right, Dr. Kim.

DR. KIM: I would say I would have a very difficult time telling families and patients who have had trial, off time, trial, trial, off trial, and have had, to the extent possible in a single individual case, good evidence for efficacy, for that person to say that the FDA knows better than they do.

DR. YANG: Understood, thank you.

Dr. Reppas.

DR. REPPAS: John Reppas.

I think that the ban, if it happens, should be prospective, not retrospective.

DR. YANG: Thank you.

Ms. Mattivi.

MS. MATTIVI: If it's banned, it should be banned. I agree with Dr. Augustine.

DR. YANG: Okay.

Dr. Richardson, all devices or just those to come?

DR. RICHARDSON: I think prospective, not retrospective.

DR. YANG: Prospective, okay.

DR. IWATA: I agree that if it is banned, it should be all current users also.

DR. YANG: Okay. And, Dr. Iwata, I'm going to ask you the question of how would you take someone off of this?

DR. IWATA: Yes. We have experience transitioning people from all different kinds of programs, and if that were the mandate, I would say six months.

DR. YANG: Okay.

All right, Dr. Green.

DR. GREEN: I would say we have to ban it for everyone. You can't determine that it's ethical for one group and not ethical for another.

DR. YANG: Okay. Do you want to offer any suggestions on -- okay, fair enough. Tough question.

Dr. Weigle.

DR. WEIGLE: I would say ban it for all, and as part of that transition period, not only with using behavioral principles that we know on how to transition in gradually, stop the use of these kinds of devices. In the meantime, I would suggest that more -- again, maybe get another team around this person to assess all the factors that could be influencing what's happening and begin other treatments while this person is being weaned from the device.

DR. YANG: Thank you.

Dr. Fost.

DR. FOST: I agree with Dr. Kim. I think it's a particularly harsh form of paternalism to tell a caring family, a competent, well-trained, respected physician that a patient who, under their care with a horrendous condition where everything else failed and seems to have gotten better, for the federal government to tell them no, you can't continue this treatment anymore; we know better than you. I would find that very objectionable.

DR. YANG: Thank you, Dr. Fost.

All right, Dr. Dorsey.

DR. DORSEY: I think I would do all that. I have, I guess, grave concerns about how it's currently being administered. I think the three things

that come out for us is that this is a device that causes pain, it's in a vulnerable population, it's done by a third party who is not trained. If those things are all still being done to the people on it, that would lead me to say for all.

DR. YANG: Thank you.

Dr. Armstrong.

DR. ARMSTRONG: Daniel Armstrong.

I think it should be applied uniformly. The transition should be one that is very carefully evaluated. In this particular case, there is clear knowledge of behavioral analytic approaches, and there are already things built in, in terms of positive behavioral support. So the question is whether you would be weaning from the patient who presented with the problems versus a patient who is being treated. However, I would put in a caveat. If that transition is not able to be accomplished and the behavior re-escalates to the point of being life threatening, mortally threatening, very high morbidity, then an application for a specific exception should be allowed for continuation.

DR. YANG: Thank you.

Dr. Bickel.

DR. BICKEL: I think all the devices should be banned, but I do believe that a compassionate exemption could be filed on a case-by-case basis for those families and for those circumstances where there's a true

benefit.

DR. YANG: Thank you.

And Dr. Miles.

DR. MILES: I think the ban should prevent all new implants. I don't think recalls are that uncommon. There should be a transition, but the transition should be two steps, first consisting of an immediate transition from these GED-3A and GED-4 down to the devices which received the original exemption. These are lower amperage devices. And the transition for each individual patient, then, should go for three to six months.

During that monitoring time, I think that the FDA should work with the facility to develop a correctly functioning monitoring of postmarketing surveillance to understand these devices and their adverse effects so that some data can be gathered off of this transition. Compassionate use can always be considered in the future. The exemption should be removed in six months, by which time the transitioning program shall be complete, at which point all the devices would be banned until new research programs can perhaps reintroduce them in the future.

DR. YANG: Thank you, Dr. Miles.

Dr. Goodman.

DR. GOODMAN: I would allow an exception for those cases in which there is significant risk of return of self-injurious behaviors resulting in significant organ or tissue injury.

DR. YANG: Thank you, Dr. Goodman.

Mr. Mikita.

MR. MIKITA: I would ban all devices. I would also encourage a six-month transition. But after six months, I would not allow exemption.

DR. YANG: Okay.

Dr. Connor.

DR. CONNOR: Jason Connor.

I feel like this is one where being a statistician actually has benefit unlike most --

(Laughter.)

DR. CONNOR: No, I do think it is very possible that the totality of the data can indicate that risks outweigh the benefits for an average patient, which means the patient on the horizon. But given it sounds like there's actually a wealth of information for individual patients who have been using this device, that on an individual level, the data could very well indicate the benefits outweigh the risks in a patient level. And I think that it's appropriate that patients be identified.

In particular, that we look at whether patients seem to have learned. Are their shocks actually low now? And if they're not, they should be removed. But we heard a lot of cases where patients are getting applications of the device very infrequently, and for them, it seems like the benefits do outweigh the risks.

DR. YANG: Okay.

So, Dr. Peña, in answer to the direct question about applying to all devices, nearly 80% of the Panel think that it should, but with some comments. My personal comment about the risks and benefits is that we've discussed the risks and benefits in the other sections, and I think that can be extrapolated for this situation.

As far as the transitioning goes, we have a number of very experienced clinicians on the committee, so I thought that was particularly important.

A couple of suggestions: One is first to transition it to the FDA-approved devices with the lower amperage. Timing is gradual, carefully, somewhere in three to six months with a team of providers that addresses more than just the SIB, that there should be overlapping treatments, and certainly within this time period, if the behavior escalates or regresses, that for a condition with significant morbidity, mortality, that this be a compassionate exemption and to be placed back on the device.

And just because I have to quote, I believe it was Dr. Fost, "harsh paternalism," I understand that it must be very hard to tell patients that have individual success that we're going to take this away from them. So, again, this issue of individualization is very important.

So, Dr. Peña, is that adequate for Question No. 5?

DR. PEÑA: Thank you. That is adequate.

DR. YANG: All right, Dr. Bowsher, our last question.

Question 6.

DR. BOWSHER: Question No. 6: Should the FDA determine not to ban these devices, the Agency may need to determine whether a clinical study could be conducted. Therefore, please discuss what concerns, if any, you may have about conducting a clinical study with these devices in either children or adults.

DR. YANG: So you saved the best for last, huh? This could go on for hours, knowing the Panel members around the table here.

So what I'm going to ask is try to very much limit your concerns to a list. I know I've heard some of them before. If you can sort of rank, prioritize them and separate them for me in terms of children and adults, it would be much appreciated. Okay.

So let's see, why don't we start with Dr. Reppas and just go around then? So, first of all, tell me concerns that you have about conducting a clinical study, and tell me if it's children or adults.

DR. REPPAS: John Reppas.

I would draw a very crisp line between the device we talked about for much of today and the therapeutic category in general. I think for the former, it will be almost impossible to design an appropriate and ethical trial for adults, for children, for anybody. What's more, this sponsor cannot pay for it. And I don't see who steps up to do it. So --

DR. YANG: Let me take it away, yeah. Let's talk about the class.

DR. REPPAS: Okay. So the class is -- I'm agnostic because the class could be anything, and so therefore, I would imagine that for the class -- you know, it's impossible to say what future technologies will look like, and that determines trial design. So I would say that there is a universe of appropriately designable trials out there for things that we don't yet -- you know, we don't know what they look like yet, but inside this category.

DR. YANG: Okay.

Ms. Mattivi, concerns regarding using aversive therapy shocking devices in this class.

MS. MATTIVI: Stimulation parameters, both from the device output standpoint as well as from the human application of that stimulus.

DR. YANG: And that would apply to both, I assume?

Dr. Richardson.

DR. RICHARDSON: Yes, I think the device needs to be redesigned. I would hate to see it banned totally because there are obvious benefits, so it would be nice to have a sponsored project to do it. But the patients involved in -- a number of patients are not going to allow that. Nobody's going to sponsor it. So I would -- I think I would -- it's a very difficult decision. I think I would allow the patients that are being treated, I would like to see a report, an extensive report, in depth report, on the

patients who have been treated.

DR. YANG: So let me ask a little more directly. Concerns that you have about --

DR. RICHARDSON: What, yes or no?

DR. YANG: No, no. Concerns that you have about such a study, of using aversive shock treatment devices in a study.

DR. RICHARDSON: I don't like the study at all. I don't like using aversive studies.

DR. YANG: Okay. Fair enough.

Dr. Iwata.

DR. IWATA: I'm not going to comment on whether it's useful to do such a study. Just concerns about doing one?

DR. YANG: Just concerns about --

DR. IWATA: Okay. I agree, stimulus parameters. There is no device. So if the FDA were interested in putting out a call for such a study, there is no device at the current time. So no one could do a study.

Second, I don't believe that there is one clinical investigator working in the area of self-injurious behavior today who would want to participate in one of those studies. So no device, no investigators.

DR. YANG: Understood.

All right, so Dr. Green.

DR. GREEN: Well, the only thing I'd like to say, if the evaluation

doesn't involve children, then we've wasted years and years, and it won't be an effective device. But, obviously, a new device, should it be developed, has to include a whole variety of aversive stimuli. Of course, I imagine there is still some aversive stimuli that are quite benign. Tickling would probably work, but there are probably a lot of other similar stimuli.

DR. YANG: Okay.

Dr. Weigle, concerns.

DR. WEIGLE: Concerns would include for both populations, children or adults, the ability to consent and to really provide true, informed consent. The ability to report and be able to explain side effects or adverse events. And the ability of the investigators to assess the level of pain that that person may be experiencing, so the stimulus parameters, as well. And the device, how much output. I mean, it sounds quite variable, so all of those factors are a concern.

DR. YANG: Certainly. Thank you, Dr. Weigle.

Dr. Fost.

DR. FOST: I think well-designed studies are needed in this condition, horrendous condition, with presently unsatisfying treatment for many people. I think they can be done on children and adults under the federal regulations. I think that things that should go into such a study have been adequately commented on by others trying to find the right threshold, appropriate supervision, and so on.

DR. YANG: Thank you.

Dr. Dorsey.

DR. DORSEY: Two thoughts. One on the condition. Given that you're having a device that causes harm, you want to make sure that it's in the condition that has substantial harm associated with it. This would be like, again, where it comes about self-injurious behavior that's substantial or aggressive behavior that's harming others.

And then second, on the study population, you want the individuals to be as autonomous as possible. So people who are able to give consent and who aren't necessarily dependent on a particular -- dependent on receiving their care in a selected environment, where they have freedom to change environments and the like. I think those are some of the concerns that are uniform across.

DR. YANG: Thank you.

Dr. Armstrong.

DR. ARMSTRONG: Daniel Armstrong.

I'm actually a little bit appalled. If this was a drug, we would have significant preclinical studies that would have used tested animal models, would have looked at dose intensity, would have actually mapped out what the potential risk was, and I would start there before I move to human subjects.

DR. YANG: Fair concern.

Dr. Bickel.

DR. BICKEL: I think there are a lot of devices that are being currently investigated for all kinds of psychiatric conditions, including direct current transcranial stimulation, alternating current/direct current stimulation, TMS. And we should be learning from their stimulus parameters and their development of procedures and to apply those same sort of approaches to any development here. Some of those studies demonstrate that the type of electrode can significantly influence pain as well as the stimulation parameters, because pain is sometimes a consequence of those procedures, as well.

I think I would prefer that studies, if they were to be conducted, first be conducted in adults. And once efficacy has been demonstrated, figure out how to translate that into children. And I would define very rigorously what treatment failure is from other conditions so that we have a clear definition of who would be appropriate for said studies.

DR. YANG: Thank you, Dr. Bickel.

Dr. Miles.

DR. MILES: A trial could be conducted in this class of devices, and I agree with Dr. Iwata, actually, on everything he said today. Should such a researcher appear, though, complex data safety monitoring would be necessary and should be external to a clinically reimbursed treatment center, a treatment center that was also the principal clinical market and the

manufacturer would have a disqualifying -- conflicts of interest as a site or sponsor for the research.

DR. YANG: Thank you, Dr. Miles.

All right, Dr. Goodman.

DR. GOODMAN: I have nothing to add.

DR. YANG: Okay.

Mr. Mikita.

MR. MIKITA: Absolutely, it can't be a clinical study and design because for all the reasons that Dr. Weigle and Dr. Dorsey have outlined, you cannot consent these vulnerable individuals. Autonomy and ethical considerations must be acknowledged and must be preserved at one point or another during this discussion --

DR. YANG: Thank you, Mr. Mikita.

Dr. Connor.

DR. CONNOR: Jason Connor.

I think I would try -- and I'm not an expert in this field, but to find patients that are perhaps capable of providing consent that exhibit self-injurious behavior but maybe aren't mentally incapacitated so that they can provide consent somewhat.

I think there are really two trials here, what we in the drug world call Phase II and Phase III, where Phase II is identifying the type of stimulus, where it should be located on the body, the severity, the protocol,

the administration; the protocol for where to start, where does it ramp up, or does it start high like current ones. And then, kind of, once that's maybe identified, the notion of a Phase III trial or pivotal trial in the device side, where -- and this would probably occur in different centers.

We have plenty of controls, and we would enroll at centers willing to participate in such a thing, and we could try to match patients on how many times they've been refractory, how many centers have they been kicked out of, what drug therapies are they refractory to, age, the type of disability, you know, other things I'm sure clinical experts can talk about that is important to match over. It absolutely should only be done in adults.

And I think, then, there are a variety of outcomes, like the number of self-injurious events; the number of ED visits and other healthcare interventions necessary both for self-injurious events and all events; the number of restraint-free days because I assume patients not getting this therapy may be restrained at other centers; the number of psycho-psychotic drug-free days; the number of days patients are capable of home visits; and really, I'm trying to get at quality of life measures here that I think are important, and quality of life is one of the things I think we heard about from patients.

Though I agree, as a statistician, that evidence is important, so I want these things to be good evidence to make sure it really is this device and not some other part of the protocol at JRC. And then the key being

appropriate adjudication of events, and in particular adjudicating events that may have happened, but a center may have a biased notch report, so there needs to be a process so that if an event happens, it's somehow identified and reported. But I think that such a trial is really hard, but it is possible, and I design really hard trials all the time, so it takes a lot of work, but I think it's possible.

DR. YANG: Thank you, Dr. Connor.

Dr. Augustine.

DR. AUGUSTINE: I agree with all of the statements that have been said so far. And I think the only thing that I have to add is a process or a path in the event that there is not a ban, in the event that there are not sponsors and investigators ready to conduct a multi-center trial with all the rigors that we've just discussed. If there's not a ban, it doesn't change a lot of what we've struggled with today in terms of there being an overall limited ability to quantify the risks and benefits.

And as we discussed on -- discussed risk and whether it's unreasonable, there was a split. As we talked about prospective versus all devices in terms of a ban, again, there was a split. And then to say yeah, it came back about compassionate use and individual success, so there's clearly a lot of uncertainty.

If there is not a ban, then I would advocate for new systematic adverse event or risk evaluation or reporting requirements where the device

is being used with independent evaluation. And I think that, again, in the absence of a ban, is something that's critically important to eventually being able to answer some of these questions about risk and benefits.

DR. YANG: Thank you.

Dr. Peavy.

DR. PEAVY: Guerry Peavy.

I think that we need to very carefully characterize the groups. In addition to some of the factors that Dr. Connor brought up, I think there would be a lot of others, as well. One concern is how difficult it would be to recruit people for the trials and then knowing how to prioritize which variables might be more important than others.

DR. YANG: Thank you, Dr. Peavy.

Dr. Stebbins.

DR. STEBBINS: Glenn Stebbins.

I think the major concerns would be coercion. And then you'd want to have clearly defined outcomes as well as clearly defined stopping rules.

DR. YANG: Thank you.

Dr. Kim.

DR. KIM: I agree with most of the comments made already, especially the one about removing conflict of interest and conducting and evaluating the data.

I do want to go on the record saying that I -- we started today with questions about the FDA's position on concerns about the ethics of conducting such a study with their interpretation of the regulations. I have tremendous concerns with the interpretation presented today, and I'd just like to go on the record that I think that there are ways of doing this that are ethically acceptable. I can't claim that that would be what the FDA would think, since I don't work for the FDA, but from an ethical analysis, I think you can do that.

DR. YANG: Okay. Thank you very much.

Dr. Peña, so in answer to No. 6 -- I'm not going to separate it between children and adults. All I can say is that the studies must include children, but there has been a suggestion brought up that other drugs, devices, start out with animal models, then adults, and then to children.

There should be a process in place if there is not a ban, it can be conducted ethically. However, there are other concerns: lack of investigators, lack of device, lack of patients because of concerns about recruitment and consent, true informed consent, and coercion, as well as conflict of interest. However, if there is, there's also concern about the device in terms of stimulus parameters.

We should learn from other devices that are out there that have already -- that are using stimulation for different reasons. Concern about the ability for these patients that are vulnerable to report adverse

events. I think that's been brought up several times today.

And then finally, last but not least, is definition of the outcomes of the device, definition of the effect, and definition of failure and quality of life are all uncertain and need to be much better addressed.

So, Dr. Peña, is that adequate for No. 6?

DR. PEÑA: Yes, thank you.

DR. YANG: Okay. So then, finally, I would like to thank the Panel for all of their patience, their input and expertise; the FDA for their presentation, their hard work in all of this; as well as the invited speakers, the guest speakers and JRC for their contributions to today's panel meeting.

I need to ask the FDA, probably Dr. Peña, do you have any final remarks?

DR. PEÑA: Sure, very brief remarks.

The FDA appreciates the Panel's discussion of this topic, as well as the input provided during the public comment session. The meeting provided valuable information and perspectives that will help inform FDA's deliberations. The FDA has not made any decision regarding whether the devices will be banned from the market. The FDA's primary concern to consider in the continued use of these devices is the safety and well being of patients receiving this therapy.

So thank you to the Panel.

DR. YANG: Thank you, Dr. Peña.

So the April 24, 2014 meeting of the Neurological Devices Panel is now adjourned.

Thank you.

(Whereupon, at 6:12 p.m., the meeting was adjourned.)

C E R T I F I C A T E

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

NEUROLOGICAL DEVICES PANEL

April 24, 2014

Gaithersburg, Maryland

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

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ED SCHWEITZER

Official Reporter