SUMMARY MINUTES

CENTER FOR DEVICES AND RADIOLOGICAL HEALTH

MEDICAL DEVICES ADVISORY COMMITTEE

GENERAL AND PLASTIC SURGERY DEVICES PANEL

October 26, 2022

9:00 a.m. EST

Attendees:

Chairperson

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

Non-Voting Members

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

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

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

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

Alan Matarasso, M.D., FA.C.S.
Past President American Society of Plastic Surgeons
Clinical Professor of Surgery, Hofstra-Northwell Health System — New York, NY

Andrea Pusic, M.D., M.H.S., F.A.C.S., F.R.S.C.
Chief, Division of Plastic and Reconstructive Surgery, Brigham and Women's Hospital
Professor of Surgery, Harvard Medical School — Boston, MA

Colleen M. McCarthy, M.D.
Plastic and Reconstructive Surgeon, Memorial Sloan Kettering Cancer Center — New York, NY

Kelly Hunt, M.D.
Professor and Chair, Dept. of Breast Surgical Oncology, University of Texas MD Anderson Cancer Center — Houston, TX

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

Mark D. Soucek, Ph.D.
Professor, Interim Director, School of Polymer Science and Polymer Engineering, University of Akron — Akron, OH

Robert F. Diegelmann, Ph.D.
Distinguished Career and Emeritus Professor, Virginia Commonwealth University School of Medicine — Richmond, VA

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

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

Temporary Non-Voting Members

Deborah Armstrong, M.D.
Professor of Oncology
Department of Oncology, Johns Hopkins University School of Medicine — Baltimore, MD

Andrew Seidman, M.D.
Medical Oncologist, Breast Medicine Service Memorial Sloan Kettering Cancer Center
Professor of Medicine, Weill Cornell Medical College — New York, NY

Melissa Fisher
President, MJF Advisory Services — Marblehead, MA

Industry Representative

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

Consumer Representative

Rachel S. Brummert
Founder, Quinolone Vigilance Foundation

Patient Representative

Melissa Fisher
President, MJF Advisory Services — Marblehead, MA

Food and Drug Administration

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

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

Candace Nalls, Designated Federal Officer

David Krause, Ph.D.
CDRH/OPEQ/OHT4, Deputy Office Director

Food and Drug Administration Presenters

Frances Wilder, Ph.D.
Regulatory Advisor, Regulation, Policy, and Guidance (RPG)

Tajanay Ki, B.S.
Biomedical Engineer – Lead Reviewer, CDRH/OPEQ/OHTIV/DHTIVB

Tek Lamichhane, Ph.D.
Senior Staff Fellow – Lead Reviewer, CDRH/OPEQ/OHTIV/DHTIVB

Min Zhang, Ph.D.
General Engineer – Lead Reviewer, CDRH/OPEQ/OHTIV/DHTIVB

Sambasiva Arepalli, Ph.D.
Chemist – Lead Reviewer, CDRH/OPEQ/OHTIV/DHTIVB

CALL TO ORDER
INTRODUCTIONS

Panel Chairperson **Dr. Hobart W. Harris** called the meeting of the General and Plastic Surgery Devices Panel to order at 9:00 a.m. He noted the presence of a quorum and stated that present members have received training in FDA device law and regulations. He stated the day's agenda: discuss and make recommendations on the classification proposals for tissue expanders and accessories, mammary sizers, wound dressings with animal-derived materials, absorbable synthetic wound dressings, and hemostatic wound dressings with or without thrombin, nail prostheses, ultrasonic surgical instruments, single-use reprocessed ultrasonic surgical instruments, and neurosurgical ultrasonic instruments

Chairperson Harris reminded the attendees that this is a non-voting meeting and asked members of the Committee to introduce themselves.

CONFLICT OF INTEREST STATEMENT
TEMPORARY-NON-VOTING MEMBER STATUS STATEMENT
GENERAL ANNOUNCEMENTS

Candace Nalls, Designated Federal Officer, announced the issue of a Conflict of Interest Waiver to Dr. Matthew Bloom for his stock ownership in the affected firm; more information is available at www.fda.gov/advisorycommittees. She announced the participation of **Dr. P. LaMont Bryant** as the Industry Representative. She introduced **Dr. Deborah Armstrong**, **Melissa Fisher**, and **Dr. Andrew Seidman** as temporary nonvoting members and Audra Harrison as the press contact.

OPEN PUBLIC HEARING

Candace Nalls read the Open Public Hearing Disclosure Process Statement and announced the receipt of four requests to speak.

Ms. Maria Gmitro spoke on behalf of the Breast Implant Safety Alliance (BISA) in support of a Class III classification to facilitate the informed consent of patients. Her full statement is available on BisaNonprofit.org.

Ms. Joan Melendez of XCELRATE UDI, Inc. implored the committee to consider patient safety and the ability to accurately document and trace mammary sizers tissue and wound dressings when determining the assignment of classification codes and to assign a minimum of Class II designation.

Dr. Bernard Lee, in a pre-recorded statement, spoke on behalf of the American Society of Plastic Surgeons (ASPS) and the Plastic Surgery Foundation (PSF), asserting that tissue expander devices are vital to ensuring access to timely, cost-effective, and safe breast reconstruction for thousands of women. He described the National Breast Implant Registry (NBIR) which captures information on all breast implant procedures, removals, and

replacements. He stated that the NBIR is committed to providing robust real-world data to ensure the safety of essential tissue expander devices for their use in breast implant surgery.

In a pre-recorded statement, **Madris Kinard** presented data on breast implant illness and cited patient education as a primary concern about the approval of these devices. She urged the FDA to ask care providers to report cases of Breast Implant Illness and different types of cancer, assign more specific problem codes to Breast Implant Illness and cancer subtypes, and to require informed consent similar to breast implants.

For questions, **Ms. Brummert** inquired if breast implant patients have access to the national database; **Dr. Scott Glasberg** represented ASPS to say there is no open access.

Ms. Block asked the Open Public Hearing speakers if they feel that mammary sizers are sufficient to be a Class II or III, and why. **Ms. Kinard** believes Class III is appropriate because breast implants were recently up-classed to Class III. **Ms. Melendez** answered Class II since it does not qualify as implantable; **Dr. Glasberg** echoed this.

Dr. Li asked about the differences between the NBIR and the MDR, and **Dr. Glasberg** clarified that NBIR has quarterly reports and continual assessments. **Ms. Kinard** emphasized that NBIR gets data from plastic surgeons specifically, highlighting a need for more uniform reporting. **Ms. Melendez** added that the real-time aspect is NBIR is crucial and expressed concerns that surgeons often do not end up reporting to the FDA if they are reporting to a different, non-FDA database.

Dr. Seidman wondered if NBIR data differentiates patients who had a temporary expander, and patients who had an implant without an expander. **Dr. Glasberg** gave an unequivocal yes.

Dr. DeLong asked if any cases of anaplastic large cell lymphoma (ALCL) are attributable directly to tissue expanders; he also inquired if the NBIR tracks tissue expanders and can be adjusted to account for Breast Implant Illness (BII) and ALCL. **Dr. McCarthy** of the PROFILE Registry asserted that indeed, detail is collected in that level and that there is no record of a patient ever developing ALCL after having a tissue expander. **Dr. Glasberg** added that the capabilities of NBIR are easily adjusted to apply to a variety of scenarios regarding tissue expander cases, not just implant cases, going forward.

Dr. Armstrong wondered if there has been tracking of patients who receive chemo, and **Dr. Glasberg** affirmed that this is part of the standard dataset.

Dr. Pusic of the NBIR clarified that reoperation is the main cause of adverse events reported, that the registry is working to incorporate more in-depth patient and symptom reporting, and that, while not all doctors are aware, NBIR does accept reports from non-plastic surgeons. She concluded by highlighting the advantages of using NBIR in a postapproval setting for ensuring patient safety.

After ensuring there were no other questions, **Chairperson Harris** officially closed the Open Public Hearing.

FDA PRESENTATON — Medical Device Classification Process

Dr. Frances Wilder announced that for this meeting, the panel is to provide input on proper classification for 10 device type, emphasizing that devices should be placed in the lowest class whose level of control provides a reasonable assurance of safety and effectiveness. She detailed the criteria for Class I, Class II, and Class III and provided examples of devices in these categories. She discussed the classification process for pre-amendments unclassified device types. The panel is to consider:

- risks to health presented by each device type;
- whether the device is life supporting, life-sustaining, or of substantial importance in preventing impairment of human health;
- if the device presents a potential and reasonable risk of illness or injury;
- whether general controls alone are sufficient to provide reasonable assurance of safety and effectiveness for each device type;
- whether sufficient information exists to develop special controls; and
- what those special controls should be to provide a reasonable assurance of safety and effectiveness for the device type.

Dr. Wilder noted that the FDA will consider all evidence presented from the public and panel, will publish a proposed rule in the Federal Register in their classification designation, and will finally issue a final rule identifying the appropriate class.

CLARIFYING QUESTIONS FROM THE PANEL

Dr. DeLong inquired about the device tracking capabilities for Class III versus Class II and if Class II can be enabled for postmarket tracking. **Dr. Dean** responded that all Class II must have Unique Device Identification tracking and **Dr. Krause** confirmed this.
Dr. Seidman asked how long manufacturers and marketers will have to submit a PMA if tissue expanders are designated Class III, to which **Dr. Dean** responded at least a year.
Dr. Armstrong wondered if devices introduced to market since 1976 have gone through PMA, or if all tissues expanders have been excluded from PMA processes thus far. She also asked if any devices currently on market would be exempt from an approval process if classified Class III. **Dr. Dean** and **Dr. Krause** confirmed that all tissue expanders have gone through the 510K process since 1976, except for one carbon dioxide expander that went through the de novo process, and that all tissue expanders intended for use in the breast would need a PMA to remain on market in the U.S.
Dr. Pusic expressed concerns that manufacturer approval timelines may create an interim period where patients do not have access to necessary tissue expanders. **Dr. Dean** agreed that this is an important consideration.
Ms. Block asked the FDA if product use is ever limited from classification changes. **Dr. Dean** replied that many devices have been up classified but successfully remained on market.

FDA PRESENTATION — Classifying Tissue Expanders and Accessories Regulated for Product Code LCJ

Tajanay Ki described unclassified devices currently under product code LCJ, including their indications for use, regulatory history, and clinical background. Importantly, tissue expanders are intended for temporary subcutaneous or submuscular implantation to develop surgical flaps or additional tissue coverage in a variety of surgical applications, such as breast reconstruction following mastectomy, treatment of underdeveloped breasts, scar revision, and treatment of tissue deformities or injuries. Indications for use depend on the intended anatomical location for the tissue expander.

Ms. Ki summarized an FDA literature review conducted between 2005 and 2022 regarding the safety of tissue expanders, particularly in breast tissue, in which the majority of outcomes involved complications, though, for breast implant associated anaplastic large cell lymphoma (BIA-ALCL) specifically, no cases were found. The reviews were limited in their ability to provide information on outcomes for use in non-breast tissue.

Ms. Ki proceeded with an overview of Medical Device Reports (MDRs), their limitations, and numbers of adverse outcomes reported by disease type. Overall, the MDR analysis shows that there are complications associated with the use of tissue expanders for all indications. The analysis shows that there are specific complications associated with the use of tissue expanders in the breast that may not be found when tissue expanders are used in other anatomical regions. In particular, the MDR analysis shows that there are several reports of BIA-ALCL and BII when tissue expanders are used in the breast.

Ms. Ki presented a discussion of Class I, Class II, and Class III recall histories for these devices. **Ms. Ki** then followed with a detailed discussion of risks to health and mitigations. For tissue expanders, the five main risk categories for the devices and for their accessories are:

- Skin trauma from device malposition or over inflation.
- Device malfunction or device failure leading to reoperation.
- Infection.
- Adverse tissue reaction.
- Pain or discomfort.

For breast-specific tissue expanders, three additional categories exist:

- The potential for a delay in cancer treatment from complications from the tissue expander use, such as infection.
- Breast implant illness (BII).
- Breast implant associated anaplastic large cell lymphoma (BIA-ALCL).

Classification Recommendations

FDA recommends Class III for tissue expanders intended for use in the breast. Insufficient information exists to determine that general and special controls assure their safety and effectiveness. Additionally, they present a potential unreasonable risk of illness or injury. The risk of BIA-ALCL and BII potentially occurring with tissue expanders intended for use in

the breast may not be mitigated by special controls. Post-market oversight is suggested to monitor devices and offer reasonable assurance of safety.

FDA recommends Class II for tissue expanders intended for use in other parts of the body, or nonbreast use. Special controls can adequately mitigate the risk to health and provide reasonable assurance of device safety and effectiveness for this device type. Recommended mitigations are performance testing, sterilization, testing and validation information, shelf life validation, biocompatibility evaluation, and labeling.

FDA recommends Class II for tissue expander accessories. Special controls can adequately mitigate the risk to health and provide reasonable assurance of device, safety, and effectiveness for tissue expander accessories. Recommended mitigations are performance testing, sterilization, testing and validation information, shelf life validation, biocompatibility evaluation, and labeling.

Definitions

A tissue expander is an inflatable silicon elastomer shell filled with normal physiological saline intended for temporary implantation to develop surgical flaps or additional tissue coverage in surgical applications. Tissue expanders may have a smooth or textured surface and are filled through an injection port. A tissue expander is intended for temporary subcutaneous or submuscular implantation not to exceed six months. The device includes tissue expanders intended for use in the breast, tissue expanders intended for use in other parts of the body, or nonbreast, and accessories for tissue expanders.

For breast: Generally round in shape and have varying fill volume range width range, height range, and projection range.. They may have multiple suture tabs for an option to suture to surrounding tissues. They are intended for breast reconstruction after mastectomy or other trauma, correction or treatment of an underdeveloped breast, treatment of soft tissue deformities, or a combined chest wall and breast deformities.

For nonbreast: Can have different shapes including rectangular, cylindrical, U shaped, and crescent. They have varying fill volumes and dimensions. They are intended for soft tissue expansion, such as scar revision and treatment of tissue deformity or injuries and anatomical locations other than the breast.

For accessories: Can include port detectors, fluid dispensing systems, needle infusion sets, external fill ports, and syringe assists.

Additionally, FDA poses these specifications:

1) Class III premarket approval when intended for use in the breast.
2) Class II special controls when intended for use in other parts of the body or nonbreast.
3) Class II special controls for tissue expanders and accessories.

Special controls

For non-breast tissue expanders:

1) The patient contacting components of the device must be demonstrated to be biocompatible.
2) Performance data must demonstrate the sterility of patient contacting components of the device.

3) Nonclinical performance testing must demonstrate that the device performs as is intended under anticipated conditions of use. The following performance characteristics must be tested.
    a. Mechanical assessment of the shell, including tensile strength, percent elongation, tensile set, and joint testing.
    b. Shell surface characterization, including manufacturing methods, surface roughness, or texturing.
    c. Injection site testing to show that tissue expander can be accurately assessed.
    d. Valve competency testing, if applicable, to demonstrate that valve integrity is maintained at in vivo loads.
    e. Self-sealing patch testing, if applicable, to demonstrate a punctured patch can self-seal and maintain that self-seal for the duration of use.
4) Performance data must support the shelf life of the device for continued sterility, package integrity, and functionality over the requested shelf life.
5) Labeling must include:
    a. Information on how the device operates in the typical course of treatment.
    b. Warning related to use beyond tissue tolerances, which may result in tissue damage.
    c. The risks and benefits associated with the use of the device.
    d. Post operative care instructions.
    e. Alternative treatments.
    f. Shelf life.

For tissue expander accessories:

1) The patient contacting components of the device must be demonstrated to be biocompatible.
2) Performance data must demonstrate the sterility of patient contacting components of the device
3) Nonclinical performance testing must demonstrate that the device performs as intended under anticipated conditions of use.
4) Performance data must support the shelf life of the device for continued sterility, package integrity, and functionality over the requested shelf life.
5) Labeling must include
    a. information of how the device accessory operates.
    b. the risks and benefits associated with the use of the device accessory.
    c. Shelf life.

CLARIFYING QUESTIONS FROM THE PANEL

Dr. Armstrong, Dr. Li, Dr. Matarasso, Dr. Ballman, and Dr. Pusic asked for highly specific data clarification/reiteration, which **Dr. Dean** and **Dr. Ashar** provided to the extent of the existent data.

FDA QUESTIONS TO THE PANEL

Question One

FDA has identified skin trauma, device malfunction, or device failure leading to reoperation, infection, adverse tissue reaction, pain or discomfort, delay in adjunctive treatment or therapies, BII and BIA-ALCL as risks to health that could result from the reported device related adverse events, including device leakage or rupture, over inflation, and inadequate sterilization.

Given tissue expanders are intended for use in the breast are intended to be temporary devices that are often replaced with permanent implants, it is unclear whether temporary exposure to tissue expanders may contribute to long-term safety risks. For example, BIA-ALCL and BII. The risk of BIA-ALCL and BII potentially incurring tissue expanders used in the breast present a potential unreasonable risk of illness or injury based on limited clinical information that has been obtained.

To the panel:

- Please comment on whether you agree with inclusion of all these risks and the overall risk assessment of tissue expanders intended for use in the breast.
- Please comment on whether you believe that any additional risks should be included in the overall risk assessment of tissue expanders intended for use in the breast.
- Please comment on whether there is reasonable assurance of safety for tissue expanders intended for use in the breast.
- Please comment on whether there was a reasonable assurance of effectiveness for tissue expanders intended for use in the breast.

Dr. Bryant asked if medical procedures are included in this risk assessment; **Dr. Dean** responded that only risks associated with the indicated device and device use are being evaluated.

Dr. Seidman expressed a concern that BII and BIA-ALCL are being grouped together too hastily.

Dr. Hunt was concerned that BIA-ALCL is inappropriately associated with expanders.

Dr. Armstrong noted that there should be an added risk for patients to understand that having this device in place could prevent them from undergoing certain diagnostics.

Dr. DeLong is concerned that the device risk is easily conflated with general reconstructive risk, and **Dr. Pusic** found this astute.

Dr. Armstrong additionally articulated concerns that the devices will see practical use for longer than six months; **Dr. Dean** responded that is beyond the indicated use.

Dr. Harris summarized the panel's contributions: general agreement with FDA's identification of risks along with some other general concerns. **Dr. Dean** deemed this acceptable.

Question Two

FDA believes that tissue expander intended for use in the breast present an unreasonable risk of illness or injury. Based on the literature search conducted and the evidence obtained from review of MDRs, several risks to health have been identified, including BII and BIA-ALCL. Given that tissue expanders for use in the breast are intended to be temporary devices that are often replaced with permanent implants, it is unclear whether temporary exposure to tissue expanders may contribute to long-term safety risks for example, BII or BIA-ALCL. Although there was very limited information from our literature search on BII and BIA-ALCL with tissue expander use in the breast, MDR reports of BII and BIA-ALCL after tissue expander use in the breast have reported or described these risks with tissue expander use. Additionally, while tissue extenders may be effective for use in breast reconstruction, there are alternatives to breast reconstruction. For example, no reconstruction, external prosthesis, autologous tissue reconstruction, or not using a tissue expander. Therefore, the risk of injury is unreasonable given the lack of probable benefit.

A) Do you agree with this assessment? If not, please explain.

FDA believes that insufficient information exists to determine that general and special controls are sufficient to provide reasonable assurance of the safety and effectiveness of tissue expanders intended for use in the breast. Given the limited available information of the long-term effects of these devices when used in the breast, FDA does not believe that special controls can be established to mitigate the known risk to health associate with these devices.

B) Do you agree with this assessment?

If you disagree, please identify the valid scientific evidence available in support of a reasonable assurance of safety and effectiveness of tissue expanders intended for use in the breast.

In addition, please identify the special controls that could be established that you believe would be sufficient to mitigate the risks of health and provide a reasonable assurance of safety and effectiveness of tissue expanders intended for use in the breast.

If you recommend a classification other than Class III for this device, please discuss your reasons.

To expedite the discussion, **Dr. Dean** requested each panel member to state their position on the recommendation of Class III.

In favor of Class II: **Dr. McGrath, Dr. Ballman, Dr. DeLong, Dr. Matarasso, Dr. Soucek, Ms. Fisher, and Dr. Bryant.**

In favor of Class III: **Dr. Galandiuk, Dr. Pusic, Dr. McCarthy, Dr. Seidman, Dr. Hunt, Dr. Li, Dr. Seidman, Ms. Block, and Ms. Brummert.**

Dr. Dean requested confirmation that the panel agrees there is a reasonable expectation of effectiveness for these devices. **Dr. Harris** provided this confirmation.

Question Three

If you agree with the risks about tissue expanders intended for use in the breast, please discuss whether these risks would also apply to other tissue expanders intended for use in the breast that use other technologies.

Dr. Harris unsuccessfully probed the panel for examples of other tissue expander technologies. Panel members found themselves lacking data to answer the question, which **Dr. Dean** deemed sufficient to proceed.

Question Four

FDA has identified the following risks to health for tissue expanders intended for use in other parts of the body or non-breast: skin trauma, device malfunction or device failure leading to reoperation, infection, adverse skin reaction, and pain or discomfort.

Please comment on whether you agree with inclusion of all the risks in the overall risk assessment of tissue expanders intended for use in other parts of the body, or non-breast, under product code LCJ.

In addition, please comment on whether you believe that any additional risks should be included in the overall risk assessment of these tissue expanders intended for use in other parts of the body, or non-breast.

Dr. Harris prompted the panel for their vote on classification for non-breast tissue expanders, but the panel was generally uncomfortable giving a response due to lack of data.

Question Five

Dr. Harris valiantly translated question five: does the panel find sufficient the special controls proposed by FDA to ensure adequate safety and effectiveness for non-breast tissue expanders, namely: biocompatibility, sterility, nonclinical testing, shelf life, and labeling?

Dr. Dean requested the panel vote on the matter of how non-breast tissue expanders should be classified.

In favor of Class II: **Dr. McGrath, Dr. Matarasso, Dr. Soucek,** and **Ms. Fisher**
In favor of Class III: **Dr. Galandiuk, Dr. McCarthy, Dr. Seidman, Dr. Armstrong, Dr. Hunt, Dr. Li, Dr. Diegelmann, Dr. Bloom, Ms. Agazie, Ms. Block,** and **Ms. Brummert**
In favor of "Same as Breast Expanders": **Dr. DeLong, Dr. Ballman,** and **Dr. Bryant**

Question Six

As it turns out, Questions Five and Six were both addressed during the discussion of Question 5.

Question Seven

Dr. Li read question seven: Please comment on whether you agree with inclusion of all the risks in the overall risk assessment of tissue expander accessories under product code LCJ. In addition, please comment on whether you believe that any additional risk should be included in the overall risk assessment of these tissue expander accessories.

Dr. Ballman is comfortable with Class II designation.

Dr. Harris ensured that no other panel members were inclined to comment before prompting the next question.

Question Eight

Dr. Dean asked the panel: does anyone disagree with a Class II designation for these accessories and the special controls?

Dr. Dean found the unanimous silence a sufficient agreement.

Question Nine

Dr. Li asked if the Panel supports FDA's proposed Class II designation for tissue expander accessories. **Dr. Dean** relayed the panel's consensus in support of Class II.

Dr. Harris broke for lunch at 1:00 p.m. and prompted the panel to return at 1:30 p.m., at which time FDA Presentations resumed.

FDA PRESENTATION — Classifying Mammary Sizers Regulated Under Product Code MRD

Tajanay Ki gave a description of mammary sizer devices, which are designed for temporary intraoperative placement in the breast pocket to assist in determining the desired breast implant shape and size for the patient prior to implantation of a breast implant during breast augmentation or breast reconstruction procedures. The indication for use is to assist the surgeon in determining the appropriate size, shape, or volume of the long-term breast implants.

Ms. Ki gave an overview of the regulatory history and clinical background of mammary sizers and detailed the results and limitations of an FDA literature review between 2012 and 2022 of the safety and effectiveness of mammary sizers, but the study quality is low with only three qualifying studies. MDR analyses show complications arising from mammary sizer usage.

Ms. Ki identified the following risks and proposed special control mitigation measures.

Risk: adverse tissue reaction. Mitigation: biocompatibility evaluation and labeling.

Risk: infection. Mitigations: sterilization testing and validation information, reprocessing validation, shelf life testing, and labeling.

Risk: risk of device malfunction leading to increased operative time. Mitigation: non-clinical performance testing and labeling.

Risk: use error/improper device use. Mitigation: labeling

FDA defined a mammary sizer as a device intended for temporary intraoperative placement to assist in determining the desired breast implant shape and size for the patient. The device consists of an elastomeric outer shell that is filled with either silicone gel or saline. Mammary sizers are not intended for implantation.
FDA proposed these devices be classified as Class II devices with special controls:

1) Nonclinical performance testing must demonstrate mechanical function and durability of the device.
2) The device must be demonstrated to be biocompatible.
3) Performance data must demonstrate the sterility of the device.
4) Performance data must support the shelf life of the device by demonstrating continued sterility and package integrity over the intended shelf life.
5) Performance data must validate the cleaning and disinfecting instructions for reusable devices.
6) Labeling must bear all information required for the safe and effective use of the device, specifically including the following:
    a. A clear description of the technological features of the device, including identification of device materials, shapes, and sizes.
    b. Information on how the device operates.
    c. Validated methods and instructions for reprocessing if the device is reusable, including the number of times the device can be re-sterilized.
    d. A warning against implantation of the device.
    e. The shelf life.
    f. Disposal instructions.

CLARIFYING QUESTIONS FROM THE PANEL

Dr. DeLong wanted to ensure that gel bleed is included in resterilization; **Dr. Dean** confirmed.

Question One

Dr. Ki read: FDA has identified the following risks to health for mammary sizers. Adverse tissue reaction, infection, device malfunction leading to increased operative time, use error/improper device use. Please comment on whether you agree with inclusion of all the risks in the overall risk assessment of mammary sizers under product code MRD. In addition, please comment on whether you believe that any additional risks should be included in the overall risk assessment of these mammary sizers.

Dr. Hunt postulated that infection risks may not be due to use of the sizer and it is difficult to differentiate causation when other implants are received from the use of a sizer. **Dr.**

Bryant agreed that much of the risk comes from the procedure and those risks are complicated to separate.

Dr. Harris heard no other questions or comments and summarized that the panel is content with the risks as outlined by FDA with concerns over procedural versus device risk.

Question Two

The panel was asked for their thoughts on whether Class II is appropriate for mammary sizers cleared under product code MRD based on their risk mitigation proposals from the presentation.

The committee had no comment. **Dr. Harris** relayed to the FDA that the lack of input suggests agreement that the proposed special controls are sufficient.

Question Three

Please discuss whether you agree with FDA's proposed classification of Class II with special controls or mammary sizers. If you do not agree with FDA's proposed classification, please provide your rationale for recommending a different classification.

Dr. Harris stated that, by deductive reasoning, since the panel is in agreement that general controls are sufficient, that the panel is also in agreement that mammary sizers should be Class II.

OPEN PUBLIC HEARING

Ms. Nalls read the Open Public Hearing Disclosure Process Statement.

Dr. Diana Zuckerman, President of the National Center for Health Research spoke for this session. She urged FDA to categorize wound dressings as Class III to ensure well-designed clinical trials and registries to determine safety and effectiveness.

The Panel had no clarifying questions, and **Dr. Harris** invited FDA to begin more presentations.

FDA PRESENTATION — Classifying wound dressings with animal derived materials regulated under product code KGN

Dr. Tek Lamichhane presented a description of wound dressings made with animal materials, their indications, uses, and limitations. Overall, FDA proposed the following regulatory framework, finding special controls necessary.

Dr. Lamichhane presented risks and mitigations:
Risk: adverse tissue reaction; mitigations: biocompatibility evaluation, pyrogenicity testing, performance testing, and descriptive information.
Risk: infection; mitigations: sterilization testing/validation information, shelf-life validation, labeling, and risk management assessment of animal derived materials.
Risk: immunological reaction; mitigations: performance testing, material characterization, risk management assessment of animal derived materials and labeling.
Risk: transmission of pathogens and parasites; mitigation: risk management assessment of animal derived materials, performing testing, and labeling.
Risk: delays in wound dealing; mitigation: performance testing and descriptive information biocompatibility evaluation and labeling.

Here is our proposed classification regulation for wound testing with animal derived materials. Part a of the regulation defines the device is follows, a wound dressing with animal derived materials consists either entirely or in part of materials such as collogen, gelatin sourced from an animal and is intended to cover and protect a wound to absorb exudate and to maintain appropriate moisture balance within the wound. Such wound dressing may be manufactured with other natural or synthetic materials to achieve the final physical state of the dressing, including sheet, gel, powder. The animal derived materials incorporated in these wound dressings are intended to provide or support the physical structure of the dressing and are not intended for biological actions related to wound healing. For example, to accelerate wound healing. A wound dressing with animal derived material doesn't contain any antimicrobials, drugs or biologics. Furthermore, we are proposing these devices be classified
FDA supports a classification of Class II devices with special controls, these controls being:

1) Performing testing and descriptive information must demonstrate the functionality of the device to achieve the specified use, including establishing the physical and chemical characteristics of the device. The following must be provided:
    a. Identity, quantification, and purpose of each component in the finished product.
    b. Specification and characterization of each component in the finished product and
    c. Specification upon final release for the finished product.
2) Performance data must demonstrate the sterility of the device.
3) The device, including any degradants, must be demonstrated to be biocompatible, non-pyrogenic and contain endotoxin level within acceptable limits.
4) Performance data must support the cell type of the device by demonstrating continued sterility, package integrity and device functionality over the identified shelf life.
5) Performance data must demonstrate that the device performs as intended under anticipated condition of use, including device degradation if applicable, and evaluation of expected worst-case conditions.

6) If the device contains materials derived from a new animal species or from manufacturing processes which cause structural changes that is denaturation or modification to the animal protein performance data, for example, patch and prick-testing, human repeat insult patch testing must demonstrate that device is not immunogenic.
7) The following information must be provided to support the safety of the animal derived materials.
    a. Documentation of the processing methods including animal species, origin, husbandry, and tissue selection, as well as methods for tissue storage, transport and quarantine that mitigate the risk of parasites and pathogens.
    b. Performance data, which demonstrates adequate removal that is clearance, or inactivation of parasites and pathogens, including bacteria, mycoplasma, fungi, viruses, and other transmissible spongiform encephalopathy agents from the final finished device.
    c. A risk management assessment for the improves of animal derived materials, which considers any probable risk associated with the presence of animal tissue in the final finished wound dressing, including pathogen and parasite infection and immunological reaction. The risk management assessment must describe how these risks are controlled and mitigated by the method of animal husbandry, tissue selection, tissue handling, manufacturing, and process controls data documenting the ability of the manufacturing and sterilization to ensure adequate removal that is clearance or inactivation of parasites and pathogens from the final finished device.
8) Labeling must include:
    a. A description of intended user population.
    b. Specific instruction regarding the proper placement, sizing, duration of use, frequency of dressing change, maximum use life per application of the dressing, maximum total use life of the dressing and removal of the dressing, if applicable.
    c. A list of each ingredient or component within the finished device, including the functional role of that ingredient or component within the device.
    d. If the device is non-resorbable, a warning statement for the potential retention of material in the wound or the surrounding area.
    e. A contraindication for any known sensitivity to components within the device.
    f. A contraindication if there are incompatibilities with other therapies.
    g. Shelf life.
    h. A statement regarding when to discontinue use of the device after multiple reapplications based on biocompatibility and performance testing, if applicable.
    i. For devices indicated for over-the-counter use, the indications must specify conditions, uses, or purposes for which the product may be safely administered by a lay user without the supervision of a licensed medical practitioner.
    j. Any statement in the labeling must be clear such that they may be understood by the end user, supported by appropriate evidence and consistent with the intended

use of covering and protecting a wound, absorbing exudate, and maintaining appropriate moisture balance within the wound.

k. Disposal instructions.

QUESTIONS FOR THE PANEL

Question One

Dr. Harris asked for the panel's thoughts on the special controls.

Dr. Dean quickly clarified that the intended use of these devices is simply to cover the wound and provide a moist environment.

Dr. Harris added his own thoughts with the disclaimer that they are influenced by interactions with manufacturers. **Dr. Harris** has concerns that there are no data regarding the effectiveness of these devices, such as how effective they are at keeping the wound moist, and he is also concerned that the proposed special controls cannot obtain the requested information in the absence of clinical testing, such as use in humans. **Dr. Harris** checked with **Dr. Dean** that clinical testing can be recommended in the special controls for Class II status. **Dr. Harris** also requested the Panel's input into why some animal materials are chosen over others.

Dr. DeLong concurred that there is not enough clinical data for effectiveness evaluations. **Dr. DeLong** also expressed that surgical mesh devices are similarly animal-derived and pointed out that these are Class II surgical implants; as such, he believes animal product-containing wound dressings for external use should be no higher than Class II.

Dr. Galandiuk agreed with **Dr. Harris**'s observations.

Dr. Dean called in **Dr. Lamichhane** to discuss more about the testing that does occur in rodents and pigs for absorbency and moisture.

Dr. Harris added that these studies do not account for human biological adverse reactions.

Dr. Dean stated that if clinical testing is added as a special control, this will be difficult to implement for devices already on the market, but that FDA is considering that comment.

Dr. DeLong added that perhaps testing requirements could be instituted when significantly different components are introduced to a given wound dressing product, but that up-classification brings access issues. **Dr. Dean** affirmed this.

Dr. Harris summarized: wound dressing products can be of questionable value; delaying treatment is clinically irresponsible; and he wants to see a rigorous demonstration of the product's performance with comparisons to other available options in order to feel secure with the proposed special controls. The panel generally agrees with the special controls with the added notion of potential clinical testing requirements.

Question Two

Please discuss whether you agree with FDA's proposed classification of Class II with special controls for wound dressings with animal derived materials. If you do not agree with FDA's proposed classification, please provide your rationale for recommending a different classification.

Dr. Harris, hearing nothing from the panelists, announced unanimous agreement that Class II classification is sufficient.

FDA PRESENTATION — Classifying absorbable synthetic wound dressing currently under product code FRO

Min Zhang: presented FDA's thoughts on absorbable synthetic wound dressings, including device descriptions, indications for use, regulatory history, literature review data. Identified risks and their mitigation measures are as follows:
Risk: toxicity; mitigation: biocompatibility evaluation, performance testing, and labeling.
Risk: adverse tissue reaction; mitigation: biocompatibility evaluation, performance testing and descriptive information, pyrogenicity testing, and labeling.
Risk: infection; mitigations: sterilization testing and validation information, shelf life validation, and labeling.
Risk: delay in wound healing; mitigation: biocompatibility evaluation, animal performance testing, performance testing, and descriptive information and labeling.
Risk: failure of device integration; mitigation: animal performance testing and labeling.

FDA proposes Class II with special controls, with special controls being:

1) Performance testing and descriptive information must demonstrate the functionality of the device to achieve the specified use, including establishing the physical and chemical characteristics of a device. The following must be provided:
    a. Identity, quantification, and purpose of each component in the finished product
    b. Specification and characterization of each component in the finished product
    c. Final release specifications for the finished product.
2) Performance data must demonstrate the sterility of the device.
3) The device including any degradants must be demonstrated to be biocompatible, nonpyrogenic, and contain endotoxin level within acceptable limits.
4) Performance data must support the shelf life of device by demonstrating continued sterility package integrity, and device functionality over the intended shelf life.
5) Animal performance testing must demonstrate that the device materials and degradants don't delay the wound healing process and can be appropriately integrated into the surrounding tissue.
6) Performance data must demonstrate that the device performs as intended under anticipated conditions of use including complete degradation of any absorbable materials in the wound and evaluation of expected worst case conditions. The labelling must include the following:
    a. A description of the intended user population.

b. Specific instructions regarding the proper placement, sizing, duration of use, frequency of dressing change
c. Maximum use life per application of the dressing
d. Maximum total use life of the dressing
e. Removal of the dressing if applicable.
f. A list of each ingredient or component within the finished device including the functional role of that ingredient or component within the device.
g. If the device has non resorbable components, a warning statement for the potential retention of those components in the wound or the surrounding area.
h. A contraindication for any known sensitivity to components within the device.
i. A contraindication if there are incompatibilities with other therapies
j. Shelf life
k. A statement regarding when to discontinue the use of the device after multiple reapplications based on biocompatibility.
l. Performance testing, if applicable.
m. Any statements in the labelling must be clear such that they may be understood by the end user supported by appropriate evidence, and consistent with the intended use of covering a wound, absorbing exudate, and maintaining appropriate moisture balance within the wound
n. Disposal instructions.

QUESTIONS FROM THE PANEL

Ms. Agazie requested more information on product functionality and animal testing, and **Dr. Diegelmann** asked about pyrogenicity testing, which **Dr. Krause** provided. **Dr. Li** wondered about biodegradability and varied absorbability for various polymers and various wound types: how can the degradation rate be matched with wound type? **Dr. Krause** said this is not specified.

FDA QUESTIONS

Question One

Please comment on whether you agree with inclusion of all the risks in the overall risk assessment of absorbable synthetic wound dressings. In addition, please comment on whether you believe that any additional risks should be included in the overall risk assessment of these absorbable synthetic wound dressings.

Dr. Hunt found toxicity to be too vague of phrasing.

Dr. Bryant again mentioned conflation between procedural risks and product risks.

Dr. Harris relayed to FDA that the panel is comfortable with the list of risks aside from the vagueness of ‘toxicity.’

Question Two

The panel was asked for their comment on the six proposed special controls.

Dr. Hunt expressed concern about material degradation timelines and requested more detail. **Dr. Li** echoed this concern due to polymer variation and biological variations, and **Ms. Block** added there are further variations due to patient age. **Dr. Soucek** thinks polymer absorption is too complicated to standardize across human beings. **Dr. Galandiuk** emphasized a need for preclinical standardized models. **Dr. DeLong** expressed concerns about deceitful marketing practices for purportedly expedited wound car, and **Dr. Dean** noted that labeling can address this issue.

Question Three

Please discuss whether you agree with FDA's proposed classification of Class II with special controls for absorbable synthetic wound dressings. If you do not agree with FDA's proposed classification, please provide your rationale for recommending a different classification.

Dr. Harris relayed the panel's unanimous silence as approval for the Class II with special controls designation and concluded the question section.

FDA PRESENTATION — Classifying topical hemostatic wound dressings that either contain or do not contain thrombin

Dr. Sambasiva Arepalli presented background, descriptions, indications, limitations, and literature review results for topical hemostatic wound dressings, which are currently unclassified, and the differences between those that do and do not contain licensed thrombin. These dressings generally help achieve hemostasis through physical means, such as creating a physical barrier to stop blood flow, leveraging the absorb to properties of the dressing material to support rapid dehydration and to concentrate platelets and clotting factors at the wound site to aid the natural coagulation cascade.

Regarding risks and mitigations:

Risk: uncontrolled bleeding; mitigation: material characterization including performance testing, shelf-life validation, labelling, and BLA approval for thrombin.
Risk: infection; mitigation: sterilization testing/validation information, shelf-life validation, labeling, risk management assessment, BLA approval for thrombin.
Risk: adverse tissue reaction; mitigation: biocompatibility evaluation, labeling, and BLA approval for thrombin.
Risk: delayed wound healing; mitigation: performance testing and descriptive information, biocompatibility evaluation, and labeling.
Risk: pathogen transmission; mitigation: risk management assessment for animal-derived materials, performance testing, labeling, and BLA approval for thrombin.
Risk: immunological reaction; mitigation: management assessment for animal derived materials, performance testing and descriptive information BLA approval for thrombin and labelling.

Risk: Microbial growth; mitigation: antimicrobial characterization and performance testing, and sterilization validation.
Risk: contribution to the spread of antimicrobial resistance; mitigation: antimicrobial characterization and performance testing AMR risk assessment and labeling.
For risks of foreign body reaction due to retained device, rebleeding after attaining hemostasis, arterial or venous embolism, and thrombosis, proposed mitigations are performance testing and labeling.

FDA proposes Class II with special controls, these being:

1) Performance testing and descriptive information must demonstrate the functionality of the device to achieve the specified use, including establishing the physical and chemical characteristics of the device. The following must be provided.
    a. Identity, quantification, and purpose of each component in the finished product.
    b. Specification and characterization of each component in the finished product.
    c. Final release specifications for the finished product.
2) For the hemostatic wound dressings with licensed thrombin, the licensed thrombin component must be licensed through approved biologics license application and must function in the device consistent with BLA approved indications and usage.
3) Performance data must demonstrate the sterility of the device.
4) The device must be demonstrated to be biocompatible.
5) Performance data must support the shelf life of the device by demonstrating continued sterility, package integrity, and device functionality over the identified shelf life.
6) Performance data must demonstrate that the device performs as intended under anticipated conditions of use, including evaluation of expected worst case conditions and must characterize
    a. amount of swelling, change in volume, or change in weight of the device.
    b. in vitro clotting time.
    c. absorption of the device under physiologically relevant conditions if the device is resorbable.
    d. in vivo time to hemostasis rate of rebleeding, failed hemostasis, effectiveness hemostasis in the presence of coagulopathy, effectiveness in patients on anticoagulation therapy if indicated uniform definition of hemostasis.
    e. Amount of device retained in that wound.
    f. Reliable adhesion to the target bleeding site for different bleeding severities.
    g. risk of thrombosis and embolization if the product contains powder or granules.
7) For devices containing animal derives materials, the following information must be provided to support the safety of the non-thrombin animal derived materials.
    a. documentation of the processing methods, including animal husbandry, using selection as well as methods for tissue storage, transport, and quarantine that mitigate the risk of parasites and pathogens.
    b. Performance data which demonstrates adequate removal, that is clearance and inactivation of parasites and pathogens including bacteria, mycoplasma, fungi,

viruses and other transmissible, spongiform and encephalopathy agents from the final finished device.

c. Risk management assessment for the inclusion of animal derived materials which considers any probable risk associated with the presence of the animal tissue in the final finished solid wound dressing including pathogen and parasite infection and immunological reaction. The risk management assessment must describe how these risks are controlled and mitigated by
    i. the methods of animal husbandry, tissue selection, and tissue handling.
    ii. manufacturing and process controls.
    iii. data documenting the ability of the manufacturing and sterilization procedures to ensure adequate removal, that is clearance and inactivation, of parasites and pathogens from the final finished device.

8) For devices containing antimicrobials, antimicrobial characterization and performance data must include the following.
    a. Performance data must demonstrate that each antimicrobial has a purpose and is present in appropriate amount to perform and intended under anticipated conditions of use and storage conditions including evaluation of worst-cast conditions.
    b. If the antimicrobial is present as a microbial barrier, microbial barrier testing must be conducted to demonstrate the inhibition of passage of microorganisms through the product.
    c. If antimicrobial is present to inhibit microbial growth within the product during use antimicrobial effectiveness testing must be conducted to demonstrate inhibition of microbial growth within the product during use. The testing must include
        i. Establishment of minimum effectiveness concentration or MEC, of the final product under worst case conditions.
        ii. Identification of the period of effectiveness, maximum product use life, based on concentration of antimicrobial, leachability data, and performance under worst case simulated conditions.
        iii. For solid topical hemostatic wounds dressings, performance evaluation should be conducted with clinically relevant strains including available strains of challenge organisms containing specific antimicrobial resistance mechanisms as parts worst case scenario performance testing. For topical hemostatic wound dressings containing antimicrobial and formulated as gel, cream, ointment, powder or granules, preservative effectiveness testing must be conducted on at least three different manufactured lots of the final finished device that has been real time aged for the stated shelf life. If the dressing is a multiple use product, the test articles should also be conditioned based on worst case simulated use for maximum use life.
    d. Evaluation and identification of any probable risk of potential contribution to the development and spread of antimicrobial resistance must include:

i. identification of each antimicrobial proposed mechanism of action and justification of its status as not medically important.
ii. AMR risk assessment for each antimicrobial including the following characterization elements, known resistance mechanisms, transmissibility of resistance, list of resistant microbial species and location of isolation or contribution to medically important antimicrobial resistance.

9) Labelling must bear all information required for the safe and effective use of the device, especially including the following.
   a. description of the intended user population.
   b. specific instructions regarding the proper placement, sizing, duration of use, frequency of dressing change, maximum use life per application of the dressing, maximum total use life of the dressing, and removal of the dressing or approximate absorption rate if applicable.
   c. instruction to inspect the wound after dressing removal to remove any residual dressing material that may be left in the wound.
   d. a list of each ingredient or component within the finished device including the functional role of ingredient or component within the dressing.
   e. if the dressing is non resorbable, the warning statement for the potential retention of material in the wound or the surrounding area.
   f. the concentration or amount of thrombin present in the product.
   g. for hemostatic wound dressings, the presence of thrombin, labeling must include warnings, precautions and contraindication indications associated with thrombin as stated in the approved BLA.
   h. Warning: severe bleeding or when vasculature is exposed, caution should be taken when using dressings in powder or granular form at the bleeding site as there is a risk of causing embolization.
   i. a contraindication for any known sensitivity with components within the dressing.
   j. a contraindication if there are incompatibilities with other therapies.
   k. a warning that the device is not intended for control of internal bleeding.
   l. shelf life.
   m. storage conditions.
   n. a statement regarding when to discontinue use of the device after multiple reapplications based on biocompatibility and performance testing if applicable.
   o. for devices indicated for over-the-counter use, the indications must specify conditions, uses, or purposes for which the product may be safely administered by a lay user without the supervision of a licensed practitioner.
   p. disposal instructions.

10) for devices containing antimicrobial, labeling must also include
   a. statement of the role of the antimicrobial in the products.
   b. specific instructions regarding how and when to properly dispose of the product and when not to use the product.
   c. a statement of general effectiveness such as antimicrobial and antibacterial or microbial barrier without listing specific test organisms or log reduction values.

d. a statement explaining the effectiveness of antimicrobial in affecting wound bioburden has not been evaluated or established.

FDA QUESTIONS

Question One

Please comment on whether you agree with inclusion of all the risks in the overall risk assessment of topical hemostatic wound dressings both without thrombin and with licensed thrombin. In addition, please comment on whether you believe that any additional risks should be included in the overall risk assessment of these topical hemostatic wound dressings.

Dr. McGrath asked for clarification on an identified risk of embolism, and **Dr. Bloom** provided the necessary medical background for this clarification and **Dr. Diegelmann** gave an example. **Dr. Bryant** requested clarification about air quality concerns and propulsion agents, which **Dr. Gibeily** provided. **Dr. Krause** provided specifications around pressure usage limitations, as well.

Those being the only contributions, **Dr. Harris** announced that the committee is comfortable with FDA's proposed list of risks.

Question Two

Please discuss whether the identified special controls for hemostatic wound dressings without thrombin appropriately mitigate the identified risks to health and whether additional or different special controls are recommended.

In the absence of comments, **Dr. Harris** announced that the panel is comfortable with the proposed special controls.

Question Three

Please discuss whether you agree with FDA's proposed classification of Class II with the special controls for a topical hemostatic wound dressing without thrombin and a topical hemostatic wound dressing with the licensed thrombin. If you do not agree with FDA's proposed classification, please provide your rationale for recommending a different classification.

Hearing no comments, **Dr. Harris** concluded that the panel is comfortable that topical hemostats both with and without licensed thrombin be classified as Class II medical devices.

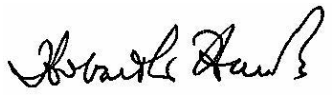
CONCLUDING REMARKS
ADJOURNMENT

Ms. Brummert, the consumer representative, **Dr. Bryant**, the industry representative, and **Ms. Fisher,** the patient representative, thanked the FDA and panel for their inclusion in these deliberations.

Dr. Krause thanked **Dr. Harris**, the representatives, and the panel members for their contributions on behalf of the FDA.

Dr. Harris thanked all the participants, FDA, and Open Public Hearing speakers for their contributions and adjourned the meeting.

I approve the minutes of this meeting as recorded in this summary.



Hobart W. Harris, M.D., M.P.H.
Chairperson

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November 8, 2022

I certify that I attended this meeting on October, 26, 2022 and that these minutes accurately reflect what transpired.

Candace J. Nalls -S

Digitally signed by Candace J. Nalls -S
Date: 2022.11.16 16:32:14 -05'00'

Candace Nalls
Designated Federal Officer