Classification of Tissue Expanders
FDA Questions

General and Plastic Surgery Devices Panel of the Medical Devices Advisory Committee

October 26-27, 2022

1. According to 21 CFR 860.7(d)(1), "there is reasonable assurance that a device is safe when it can be determined, based upon valid scientific evidence, that the probable benefits to health from use of the device for its intended uses and conditions of use, when accompanied by adequate directions and warnings against unsafe use, outweigh any probable risks. The valid scientific evidence used to determine the safety of a device shall adequately demonstrate the absence of unreasonable risk of illness or injury associated with the use of the device for its intended uses and conditions of use." In addition, according to 21 CFR 860.7(e)(1), "there is reasonable assurance that a device is effective when it can be determined, based upon valid scientific evidence, that in a significant portion of the target population, the use of the device for its intended uses and conditions of use, when accompanied by adequate directions for use and warnings against unsafe use, will provide clinically significant results."

    a. Please address the following questions regarding the risks to health posed by tissue expanders intended for use in the breast:

        i. FDA has identified the following risks to health for tissue expanders intended for use in the breast based upon literature and our search of adverse events submitted through Medical Device Reports (MDRs):

Identified Risk	Description/Examples
Skin trauma	Device malposition or over inflation with saline may lead to skin trauma such as necrosis, thinning, sloughing, and extrusion.
Reoperation resulting from device malfunction or device failure	Device malfunction, such as rupture/leakage, over inflation or failure to inflate, may require reoperation or explantation. Additional risks associated with reoperation include anesthesia risk, surgical time operation, patient dissatisfaction, infection, delay in treatment, scarring, and psychological burden.
Infection	Inadequate device sterilization or packaging integrity may lead to infection that may lead to additional surgical procedures.

Adverse tissue reaction	Device material(s) may elicit adverse tissue reactions, such as allergic reaction, toxicity, and foreign body response.
Pain or discomfort	This can result from device usage.
Delay in adjunctive treatment or therapies	The potential to delay chemotherapy or other adjunctive cancer treatment/therapies to resolve any potential complications from the tissue expander use, such as infection.
Breast Implant Illness (BII)	Breast Implant Illness may develop from the implantation/presence of tissue expander in the breast.
Breast Implant-Associated Anaplastic Large Cell Lymphoma (BIA-ALCL)	Breast Implant- Associated Anaplastic Large Cell Lymphoma may develop from the implantation/presence of tissue expander in the breast.

The identified risks could result from the reported device-related adverse events including device leakage/rupture, over inflation, and inadequate sterilization.

Please comment on whether you agree with inclusion of all these risks in the overall risk assessment of tissue expanders intended for use in the breast. In addition, 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.

ii. Given the available information, please comment on whether there is reasonable assurance of safety for tissue expanders intended for use in the breast.

b. While the literature information focused on safety, tissue expanders can be effective for use in breast reconstruction and may offer benefits including delayed reconstruction and flexibility with oncological treatments. Tissue expanders have also been cleared for correction or treatment of an underdeveloped breast, or treatment of soft tissue deformities or a combined chest wall and breast deformities. Please comment on whether there is a reasonable assurance of effectiveness for tissue expanders intended for use in the breast.

2. Section 513 of the Food, Drug, and Cosmetic Act states a device should be Class III if:
   - insufficient information exists to determine that general and special controls are sufficient to provide reasonable assurance of its safety and effectiveness, AND

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

A device should be Class II if:

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

A device should be Class I if:

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

OR

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

BUT

I. is not purported or represented to be for a use in supporting or sustaining human life or for a use which is of substantial importance in preventing impairment of human health, and

II. does not present a potential unreasonable risk of illness or injury.

Please discuss the following questions:

a. FDA believes that tissue expanders 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 (e.g., BII, 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/described these risks with tissue expander use. Additionally, while tissue expanders can be effective for use in breast reconstruction, there are alternatives to breast reconstruction (e.g., 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. Do you agree with this assessment? If not, please explain why.

b. 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 on 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 risks to health associated with these devices. Do you agree with this assessment?

If you disagree with this assessment, 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 to health and provide a reasonable assurance of safety and effectiveness of tissue expanders intended for use in the breast.

In accordance with 21 CFR 860.10(a), if you recommend a classification other than class III for this device, please discuss the reasons for your recommendation.

3. If you agree with the risks above for 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, regardless of technological characteristics.

4. FDA has identified the following risks to health for tissue expanders intended for use in other parts of the body (non-breast):

Identified Risk	**Description/Examples**
Skin trauma	Device malposition or over inflation with saline may lead to skin trauma such as necrosis, thinning, sloughing, and extrusion.
Reoperation resulting from device malfunction or device failure	Device malfunction, such as rupture/leakage, over inflation or failure to inflate, may require reoperation or explantation. Additional risks associated with reoperation include anesthesia risk, surgical time operation, patient dissatisfaction, infection, delay in treatment, scarring, and psychological burden.
Infection	Inadequate device sterilization or packaging integrity may lead to infection that may lead to additional surgical procedures.
Adverse tissue reaction	Device material(s) may elicit adverse tissue reactions, such as allergic reaction, toxicity, and foreign body response.
Pain or discomfort	This can result from device usage.

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 (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 (non-breast).

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

    A device should be Class II if:
    - general controls by themselves are insufficient to provide reasonable assurance of the safety and effectiveness, AND
    - there is sufficient information to establish special controls to provide such assurance.

    A device should be Class I if:
    - general controls are sufficient to provide reasonable assurance of the safety and effectiveness

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

    BUT

    I. is not purported or represented to be for a use in supporting or sustaining human life or for a use which is of substantial importance in preventing impairment of human health, and

    II. does not present a potential unreasonable risk of illness or injury.

    FDA believes general controls by themselves are insufficient to provide reasonable assurance of the safety and effectiveness and sufficient information exists to establish special controls to adequately mitigate the risks to health and provide reasonable assurance of device safety and effectiveness for this device type. As such, FDA believes that Class II is the appropriate classification for tissue expanders intended for use in other parts of the body (non-breast). Following is the risk/mitigation table which outline the identified risks to health for these devices and the recommended controls to mitigate the identified risks.

    Risk/mitigation recommendations for tissue expanders intended for use in other parts of the body (non-breast) under product code "LCJ"

Identified Risk	Recommended Mitigation Measure
Adverse tissue reaction	Biocompatibility evaluation Labeling

Identified Risk	Recommended Mitigation Measure
Skin trauma	Performance testing Labeling
Reoperation resulting from device malfunction or device failure	Performance testing Labeling
Infection	Sterilization testing/validation/information Shelf-life validation Labeling
Pain or discomfort	Labeling

Please discuss whether the identified special controls for tissue expanders intended for use in other parts of the body (non-breast) appropriately mitigate the identified risks to health and whether additional or different special controls are recommended:

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. Non-clinical performance testing must demonstrate that the device performs as intended under anticipated conditions of use. The following performance characteristics must be tested:
    a. Mechanical assessment of the shell (tensile strength, percent elongation, tensile set, and joint testing).
    b. Shell surface characterization (manufacturing methods, surface roughness/texturing)
    c. Injection site testing to show that tissue expander can be accurately accessed.
    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 and the typical course of treatment.
    b. Warning related to use beyond tissue tolerance 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.

6. **Please discuss whether you agree with FDA's proposed classification of Class II with special controls for tissue expanders intended for use in other parts of the body (non-breast). If you do not agree with FDA's proposed classification, please provide your rationale for recommending a different classification.**

7. FDA has identified the following risks to health for tissue expanders accessories:

Identified Risk	Description/Examples
Skin trauma	Needle injection may lead to minor bruising, bleeding, or other injury to tissue. Inaccurate reading from port detector may lead to bleeding if injection made at wrong location.
Device malfunction leading to increased operative time	Inaccurate reading from port detector may lead to rupture/leakage of tissue expander or damage/bleeding to surrounding blood vessels or tissues if injection made at wrong location. Needle misalignment may lead to rupture/leakage of tissue expander if needle is inserted at incorrect angle. These examples may lead to increased operative time and additional risks, such as increased anesthesia.
Infection	Inadequate device sterilization or packaging integrity may lead to infection that may lead to additional surgical procedures.
Adverse tissue reaction	Device material(s) may elicit adverse tissue reactions, such as allergic reaction, toxicity, and foreign body response.
Pain or discomfort	This can result from device accessory usage.

Please comment on whether you agree with inclusion of all the risks in the overall risk assessment of <u>tissue expander accessories</u> 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 expander accessories.

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

    A device should be Class II if:
    - general controls by themselves are insufficient to provide reasonable assurance of the safety and effectiveness, AND

- there is sufficient information to establish special controls to provide such assurance.

A device should be Class I if:

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

OR

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

BUT

I. is not purported or represented to be for a use in supporting or sustaining human life or for a use which is of substantial importance in preventing impairment of human health, and

II. does not present a potential unreasonable risk of illness or injury.

FDA believes general controls by themselves are insufficient to provide reasonable assurance of the safety and effectiveness and sufficient information exists to establish special controls to adequately mitigate the risks to health and provide reasonable assurance of device safety and effectiveness for this device type. As such, FDA believes that Class II is the appropriate classification for tissue expander accessories. Following is the risk/mitigation table which outline the identified risks to health for these devices and the recommended controls to mitigate the identified risks.

Risk/mitigation recommendations for tissue expander accessories under product code "LCJ"

Identified Risk	**Recommended Mitigation Measure**
Skin trauma	Performance testing Labeling
Increased operative time due to device malfunction	Performance testing Labeling
Infection	Sterilization testing/validation information Shelf-life validation Labeling
Adverse tissue reaction	Biocompatibility evaluation Labeling
Pain or discomfort	Labeling

Please discuss whether the identified special controls for tissue expander accessories appropriately mitigate the identified risks to health and whether additional or different special controls are recommended:

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. Non-clinical 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:
    i. Information on how the device accessory operates.
    ii. The risks and benefits associated with the use of the device accessory.
    iii. Shelf life.

9. **Please discuss whether you agree with FDA's proposed classification of Class II with special controls for <u>tissue expander accessories</u>. If you do not agree with FDA's proposed classification, please provide your rationale for recommending a different classification.**