Classification of Tissue Expanders and Accessories Under Product Code "LCJ"

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Device Description

- Tissue expanders and accessories are intended for temporary subcutaneous or submuscular implantation to develop surgical flaps or additional tissue coverage in a variety of surgical applications
- Intended for temporary implantation not to exceed 6 months.
- Used in various anatomical locations: breast, head, neck, calf, and others
- Composed of inflatable silicone elastomer outer shell with an injection port.
- Available in many different shapes, sizes, volume ranges, dimensions, and surface texture (e.g., smooth, textured).
- Tissue expanders also have accessories such as port detectors, fluid dispensing systems, needle infusion sets, and external fill ports or syringe assists.

Indications for Use: Breast Use

Tissue expanders have been cleared as prescription use devices for the following indications for use:

For use specific to the breast:

- Breast reconstruction after mastectomy or other trauma
- Correction or treatment of an underdeveloped breast
- Treatment of soft tissue deformities
- Combined chest wall and breast deformities

Indications for Use: Non-breast Use

Tissue expanders have been cleared as prescription use devices for the following indications for use:

For specific non-breast indications:

- Limb reconstruction
- Scar revision
- Tissue defect procedures: congenital deformities, cosmetic defects
- Correction of burn sequelae, baldness surgery, facial tumors, moles, and other skin blemishes
- Expand tissue to aid in the primary closure of defects such as nevi and lesions, and to recruit additional tissue within a designed adjacent flap by expansion
- Tattoo and other anomaly removal
- Facial reconstruction, and treatment of decubitus ulcer

Some tissue expanders may include indications for breast and non-breast use.

Indications for Use: Accessories

Tissue expander accessories have been cleared as prescription use devices for the following indications for use:

For tissue expander accessories:

- Detecting the location of the remote injection port or integral injection port
- Assisting the clinician in delivery of sterile saline into the surgically-placed, sub-dermal, temporary, removable tissue expander

Regulatory History

- Tissue expanders and accessories are a pre-amendment, unclassified device type (i.e., have been in commercial distribution prior to May 28, 1976.)
- Currently these devices are being regulated through the 510(k) pathway and are cleared for marketing if their intended use and technological characteristics are “substantially equivalent” to a legally marketed predicate device. Since these devices are unclassified, there is no regulation associated with the product code.
- To date, the FDA has cleared 48 tissue expanders and accessories under the LCJ product code. (42 tissue expanders and 6 accessories)

Regulatory History

- August 26, 2005 - Advisory Committee to discuss classification of tissue expanders.
- Identified risks: skin trauma, device failure, infection, adverse tissue reaction, and pain.
- Mitigation measures: labeling, preclinical testing, sterility, and biocompatibility.
- Panel recommendation - Class II with special controls and requiring 510(k) premarket notification.

Regulatory History

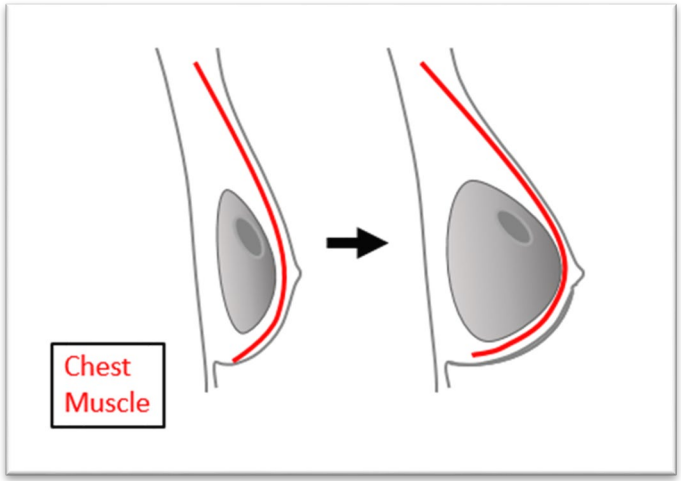
- Since 2005, there have been new developments in implant-based breast reconstruction, including new knowledge of potential risks to health (Breast Implant-Associated Anaplastic Large Cell Lymphoma (BIA-ALCL) and Breast Implant Illness (BII))

- On July 24, 2019, the FDA requested that Allergan, the manufacturer of a specific type of textured implant, recall specific models of its textured breast implants and textured tissue expanders from the U.S. market due to the risk of BIA-ALCL.

- Considering significant developments with respect to new risks related to use of breast implants and tissue expanders intended for breast reconstruction, FDA is convening this classification panel to discuss current landscape of product technology, indications for use, safety and effectiveness, and risks to health, on which to base classification of tissue expanders.

Clinical Background

- Overall Use: Tissue expanders are intended for temporary subcutaneous or submuscular implantation near the area to be repaired.
- Breast Use



- Used in other anatomical regions - head, neck, and calf.

Clinical Background

Patient Outcomes

- Based on a combination of clinical parameters
  - amount of skin or tissue stretched
  - ability of the tissue to accommodate an implant
  - tissue necrosis

- Alternatives for all expanders use can include:
  - no reconstruction
  - external prosthesis,
  - autologous tissue reconstruction,
  - not using a tissue expander

- Alternatives for breast use:
  - direct breast implant

Literature Review

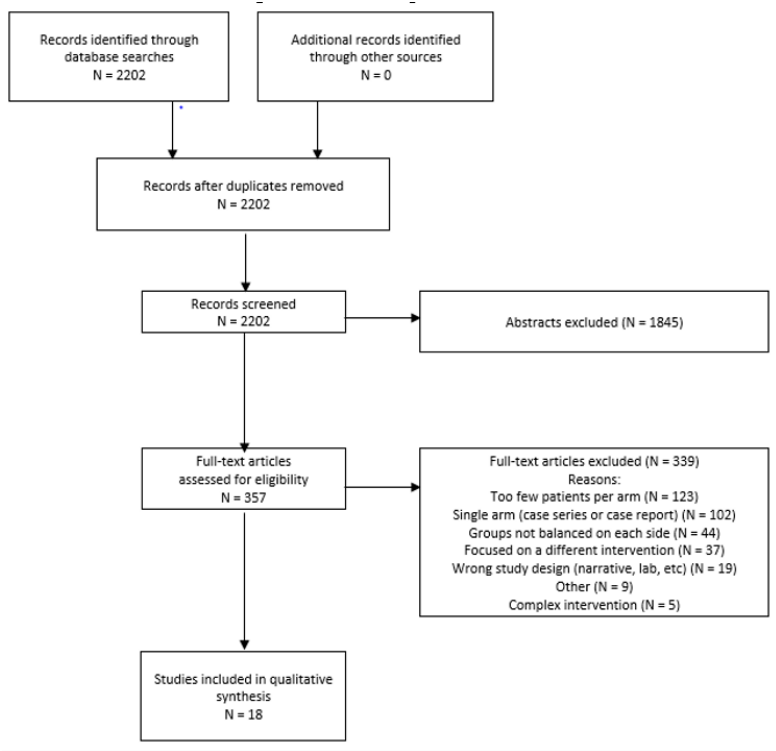
- A systematic literature review was conducted in an effort to gather any published information regarding the safety of tissue expanders and accessories under product code “LCJ.”

- Literature searches were conducted to identify any relevant articles published between April 1, 2005, and April 1, 2022.

- The searches were limited to publications in English and excluded laboratory studies, animal studies, economic and cost-effectiveness analyses, non-clinical trials (narrative reviews, conference abstracts, editorials, etc.), case series/single-arm studies (≥10 patients), and case reports (≤9 patients).

Literature Review

- The searches yielded 2,022 initial literature references. After removing articles not related to breast implant sizers based on a review of the title and abstracts, the literature search databases yielded 357 literature references.
- A total of 18 published literature references were determined to be relevant to the safety and/or effectiveness of tissue expanders (17 in breast and 1 in dentistry).
- Because tissue expanders have not been cleared for use in dental areas, the single study that examined tissue expanders in dentistry was excluded from analysis.
- 17 literature articles (studies) were reviewed for the purposes of this literature search.



Literature Review – Safety Assessment

Search methodology identified literature reporting on the following adverse events related with the use of tissue expanders.

Complication/Adverse Event in Breast Reconstruction	Number of Studies where Complication was Reported	Adverse Event Rate or Rate Range Reported in Study
Infection	12/17	71%
Explantation	9/17	53%
Skin trauma	8/17	47%
Unspecified infection	5/17	0.7%-7.1%
Mastectomy flap necrosis	6/17	1.9%-8.5%
Reoperation	6/17	35%
Seroma	6/17	0.71-7.1%
Device failure	5/17	29.5%
Hematoma	4/17	0%-2.2%
Surgical site infection (SSI)	4/17	0.6%-56.0%

Literature Review – Effectiveness Assessment

- Tissue expanders were used for expansion; however, the articles did not report the overall effectiveness.

Literature Review – Summation

- No articles provided information on tissue expander use in non-breast locations
- Search Limitations:
  - Study design
  - Exclusion of case report studies
  - Study funding sources
- 17 articles reporting on tissue expanders used in the breast
- Search supports there are additional risks associated with use of tissue expanders in the breast

Literature Review – Additional Search

- There were no BIA-ALCL cases found in the 17 included studies for tissue expanders in the breast.

- Among the excluded articles, one study evaluated BIA-ALCL patients at a single institution in a prospective manner to report patient presentation, clinical course, treatment, and outcomes (use of tissue expander not fully provided in article).

Literature Review – Additional Search

- Search for cases of ALCL with medical devices other than breast implants.
- Prior search showed ALCL in:
  - Metal implants
  - PTFE polymer vascular graft
  - gluteal implants
  - lap band
- Current search:
  - Metal femoral rod and fixation screws
  - Gluteal implant
- Reports provide additional evidence of non-breast implant-related ALCL, warrant ongoing surveillance

Medical Device Reports

- Medical Device Reporting (MDR): the mechanism for the FDA to receive significant medical device adverse events from:
  - mandatory reporters (manufacturers, importers and user facilities)
  - voluntary reporters (health care professionals, patients, consumers)

Medical Device Reports

- MDR reports can be used effectively to:
  - Establish a qualitative snapshot of adverse events for a specific device or device type
  - Detect actual or potential device problems used in a “real world” setting/environment, including:
    - rare, serious, or unexpected adverse events
    - adverse events that occur during long-term device use
    - adverse events associated with vulnerable populations
    - off-label use
    - user error

Medical Device Reports

- Limitations
  - Under reporting of events
  - Potential submission of incomplete, inaccurate, untimely, unverified, or biased data
  - Incidence or prevalence of an event cannot be determined from this reporting system alone
  - Confirming whether a device actually caused a specific event can be difficult based solely on information provided in a given report
  - MAUDE data does not represent all known safety information for a reported medical device

Medical Device Reports

- MAUDE (Manufacturer And User Facility Device Experience) Database reviewed for product code "LCJ"(tissue expander and accessories) with no date limitation through April 1, 2022
- The search resulted in the identification of 3,068 unique MDRs, including:
  - 2,544 serious injury, 509 malfunctions, 5 death, & 10 MDRs blank/other.
  - 3,052 report use in the breast, 16 report use in other anatomical locations.
- There were no MDRs on accessories associated with tissue expanders.
- The 5 death MDRs included:
  - 4 deaths (1 with event narrative, 1 with patient history, and 2 no narrative)
- There were 5,573 serious injury MDRs for the product code LCJ that were received through the Alternate Summary Reporting (ASR) Program from June 9, 2000 to December 5, 2018
  - The adverse events reported through ASR program were similar to adverse events reported through MAUDE database

Serious Injury/Tissue Expander used in Breast

Serious Injury	MDRs
Deflation/Rupture/Leak	1,475
Infection	298
Defective	170
Seroma	68
No event narrative	56
Capsular Contracture	55
Pain	40
Systemic Symptoms, Breast Implant Illness (BII)	**30**
Inflammation (cellulitis, dermatitis, and mastitis)	32
Necrosis	23
Extrusion	16
User Error	13
Foreign body contamination	12
BIA-ALCL	**8**
Hematoma	8
Allergic response	7
Autoimmune disease	6
Abscess	5
Exposure	5
Lymphedema	3

Serious Injury/Tissue Expander used in Breast

- BII
  - 30 MDRs reported systemic symptoms/ BII.
  - Reports included description of symptoms (fatigue, brain fog, chronic pain, rashes, itching, and others). Many reports reported symptoms improved/resolved when tissue expanders were explanted
- BIA-ALCL
  - 8 MDRs reported BIA-ALCL diagnosis after use of a tissue expander for breast.
    - 5 MDRs describe use of textured tissue expander followed by permanent breast implant
    - 1 MDR describes use of a textured tissue expander with no additional information on the history of other devices implanted,
    - 1 MDR describes use of a breast implant with no additional information on history of other devices implanted,
    - 1 MDR describes use of textured expanders followed by smooth implants.
- Unclear whether temporary exposure to tissue expanders may contribute to long term safety risks such as BIA-ALCL and BII

Malfunction/Tissue Expander used in Breast

Malfunction	MDR Count
Deflated, rupture, leak	262
Defective	131
Foreign body	33
Use error	11
Literature	5
Infection	4
Capsular Contracture	4

Medical Device Reports

- Of the 3,068 unique MDRs, there were 16 reports of use in other anatomical locations (non-breast)

- 16 Adverse events: 13 Serious Injury and 3 Malfunctions
  - 12 Deflation
  - 3 Infection
  - 1 No information

- These 16 MDRs for tissue expanders used in anatomical locations other than the breast did not report systemic symptoms or any type of lymphoma.

MDR Review Conclusion

- MDR analysis shows that there are complications associated with the use of tissue expanders for all indications.

- 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:
  - Including reports of BIA-ALCL and BII when tissue expanders are used in the breast.

Recall History

- The Medical Device Recall database contains medical device recalls classified since November 2002.
- Since January 2017, it may also include correction or removal actions initiated by a firm prior to review by the FDA.
- The status is updated if the FDA identifies a violation and classifies the action as a recall and again when the recall is terminated.
- FDA recall classification (resulting in the posting date) may occur after the firm recalling the medical device product conducts and communicates with its customers about the recall.

Recall History

- Recalls are classified numerical designation I, II, or III (relative degree of health hazard presented)
  - A Class I recall is a situation in which there is a reasonable probability that the use of, or exposure to, a violative product will cause serious adverse health consequences or death.
  - A Class II recall is a situation in which use of, or exposure to, a violative product may cause temporary or medically reversible adverse health consequences or where the probability of serious adverse health consequences is remote.
  - A Class III recall is a situation in which use of or exposure to a violative product is not likely to cause adverse health consequences.

Recall History

- A review of the Medical Device Recall Database found ten recalls for devices reviewed for product code "LCJ" (not time restricted):
  - Four class I recalls were initiated due to FDA's updated global safety information concerning the higher incidence of BIA-ALCL in patients who have textured breast implants
  - Two class II recalls were initiated due to certain tissue expanders that may be packaged in boxes labeled for another model.

Recall History

- A review of the Medical Device Recall Database found ten recalls for devices reviewed for product code “LCJ” (not time restricted):
  - Two class II recalls were initiated due to certain tissue expanders that may be packaged in boxes labeled for wrong size.
  - Two class II recalls were initiated due to certain tissue expanders that were shipped beyond the product shelf life.

Risks – All Tissue Expanders

- FDA has identified the following risks to health associated with all tissue expanders:

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.
Device malfunction or device failure leading to reoperation	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.

Risks - Breast Tissue Expanders

- FDA has identified the following additional risks to health associated with tissue expanders that are used in the breasts:

Identified Risk	Description/Examples
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 has been reported following 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.

Risks – Breast Tissue Expanders

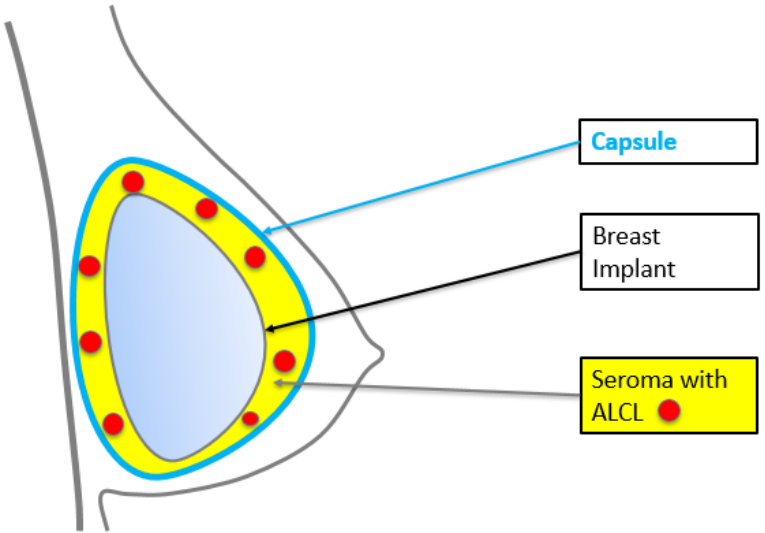
Breast Implant Illness (BII)

- Some women have reported a variety of systemic symptoms following reconstruction or augmentation with breast implants, with or without prior implantation of tissue expanders.
- “BII” has been used to describe these symptoms.
- BII was discussed at the 2019 Panel Meeting.
- Research continues to be performed to better understand any potential association with breast implants and tissue expanders.
- BII is not recognized as a formal medical diagnosis.

Risks – Breasts Tissue Expanders

Breast Implant Associated Anaplastic Large Cell Lymphoma (BIA-ALCL)

- In 2011, FDA identified a possible association between breast implants and the development of ALCL.
- In 2016, the World Health Organization designated breast implant-associated anaplastic large cell lymphoma as a T-cell lymphoma that can develop following breast implants.



Risks – Breasts Tissue Expanders

Breast Implant Associated Anaplastic Large Cell Lymphoma (BIA-ALCL)

- Tissue expanders and breast implants often have similar constructions.
- Unclear whether temporary exposure to tissue expanders may contribute to long term safety risks (e.g., BIA-ALCL, BII).
- Because average time from implantation to BIA-ALCL diagnosis is 8 to 10 years and tissue expanders are not intended for implantation beyond 6 months, inherent timeframe of BIA-ALCL pathogenesis may preclude case reports of tissue expanders present at the time of BIA-ALCL diagnosis.
    - Thus, direct correlation between tissue expanders and BIA-ALCL diagnosis may be difficult to establish.
- FDA in collaboration with the American Society of Plastic Surgeons, established a registry referred to as the PROFILE registry (Patient Registry and Outcomes For breast Implants and anaplastic large cell Lymphoma etiology and Epidemiology) to gather additional information on BIA-ALCL
- Additional research is needed on devices that are intended to be implanted into the breast to assess for any possible relation to BIA-ALCL.

Risks - Accessories

- FDA has identified the following risks to health associated with accessories to tissue expanders:

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.

Risks and Mitigations

Tissue Expanders Intended for Use in the Breast

- Unclear whether temporary exposure to tissue expanders may contribute to long term safety risks (e.g., BIA-ALCL, BII).

- The risks of BIA-ALCL and BII potentially occurring with tissue expanders intended for use in the breast may not be mitigated by special controls.

- Ability to have more stringent postmarket oversight typically associated with class III devices recommended.

Risks and Mitigations

Tissue Expanders Intended for Use in the Breast (cont'd)

Proposed Classification: Class III, PMA devices

FDA proposes that tissue expanders intended for use in the breast meet the statutory definition of a Class III device because:

- insufficient information exists to determine that general and special controls are sufficient to provide reasonable assurance of their safety and effectiveness; and

- tissue expanders intended for use in the breast present a potential unreasonable risk of illness or injury based on limited clinical information that has been obtained.

Risks and Mitigations

FDA has identified the following mitigations for tissue expanders intended for use in other parts of the body (non-breast use):

Identified Risk	**Recommended Mitigation Measure**
Skin trauma	Performance testing Labeling
Device malfunction or device failure leading to reoperation	Performance testing Labeling
Infection	Sterilization testing/validation/information Shelf-life validation Labeling
Adverse tissue reaction	Biocompatibility evaluation Labeling
Pain or discomfort	Labeling

Risks and Mitigations

FDA has identified the following mitigations for tissue expander accessories:

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

Proposed Classification

878.3505 Tissue Expanders

(a) *Identification.* A tissue expander is an inflatable silicone 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 6 months. The device includes tissue expanders intended for use in the breast, tissue expanders intended for use in other parts of the body (non-breast), and accessories for tissue expanders.

Proposed Classification

878.3505 Tissue Expanders

(1) Tissue expanders intended for use in the breast are 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 tissue. 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.

Proposed Classification

878.3505 Tissue Expanders

(2) Tissue expanders intended for other use in other parts of the body (non-breast) can have different shapes including rectangular, cylindrical, U-shaped, and crescent. They have varying fill volumes and dimensions. Tissue expanders for other parts of the body (non-breast) are intended for soft tissue expansion, such as scar revision, and treatment of tissue deformities or injuries, in anatomical locations other than the breast.

(3) Accessories common to tissue expanders in the breast and other anatomical areas can include port detectors, fluid dispensing systems, needle infusion sets, external fill ports, and syringe assists.

Proposed Classification

878.3505 Tissue Expanders

(b) Classification.

(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 (non-breast).

(3) Class II (special controls) for tissue expanders and accessories.

Proposed Special Controls

(2) Class II (special controls) when intended for use in other parts of the body (non-breast). The special controls for this device are:

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:
i) Mechanical assessment of the shell (tensile strength, percent elongation, tensile set, and joint testing).
ii) Shell surface characterization (manufacturing methods, surface roughness/texturing)
iii) Injection site testing to show that tissue expander can be accurately accessed.
iv) Valve competency testing (if applicable) to demonstrate that valve integrity is maintained at in vivo loads.
v) 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:
i) Information on how the device operates and the typical course of treatment.
ii) Warning related to use beyond tissue tolerance which may result in tissue damage.
iii) The risks and benefits associated with the use of the device.
iv) Post-operative care instructions.
v) Alternative treatments.
vi) Shelf life.

Proposed Special Controls

(3) Class II (special controls) for tissue expanders accessories. The special controls are:

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.

Thank You

Questions to Panel - LCJ

Tajanay Ki, Lead Reviewer, OHT4

Question 1 to Panel

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.”

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.”

Question 1a to Panel

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

Question 1a to Panel

(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)

Question 1a to Panel

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.
Device malfunction or device failure leading to reoperation	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.

Question 1a to Panel

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.

Question 1a to Panel

- The identified risks could result from the reported device-related adverse events including device leakage/rupture, over inflation, and inadequate sterilization.
- Given tissue expanders 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 (e.g., BIA-ALCL, BII).
- The risks of BIA-ALCL and BII potentially occurring with tissue expanders used in the breast present a potential unreasonable risk of illness or injury based on limited clinical information that has been obtained.

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.

Question 1a to Panel

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

Question 1b to Panel

(b) While the literature information focused on safety, tissue expanders may 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.**

Question 2 to Panel

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

Question 2 to Panel

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

Question 2a to Panel

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 may 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.**

Question 2b to Panel

Please discuss the following questions:

(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.

Question 3 to Panel

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.

Question 4 to Panel

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

Question 4 to Panel

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.
Device malfunction or device failure leading to reoperation	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.

Question 4 to Panel

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).

Question 5 to Panel

- 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
  - the device is purported or represented to be for a use in or 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.

Question 5 to Panel

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

Question 5 to Panel

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.

Question 5 to Panel

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
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

Question 5 to Panel

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:

Proposed Special Controls

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.

Question 5 to Panel

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:

Proposed Special Controls

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.

Question 6 to Panel

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

Question 7 to Panel

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.

Question 7 to Panel

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 risks should be included in the overall risk assessment of these tissue expander accessories.

Question 8 to Panel

- 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
  - the device is purported or represented to be for a use in-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.

Question 8 to Panel

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

Question 8 to Panel

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.

Question 8 to Panel

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

Question 8 to Panel

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.

Proposed Special Controls

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.

Question 9 to Panel

Please discuss whether you agree with FDA's proposed classification of Class II with special controls for tissue expander accessories.

If you do not agree with FDA's proposed classification, please provide your rationale for recommending a different classification.

End of Panel Questions for Product Code “LCJ”

Tajanay Ki, Lead Reviewer, OHT4