Classification of Mammary Sizer Under Product Code "MRD"

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Device Description

- Mammary sizers (also known as breast implant sizers) are intended 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

- Mammary sizers are generally constructed with an elastomeric outer shell (e.g., silicone, polyurethane) and can be filled with either silicone gel or saline.

- Mammary sizers are available in a range of diameters, projections and volumes to match the range of breast implants they intend to approximate.

- Some mammary sizers are intended for single use, while others may be re-sterilized and re-used.

Indications for Use

These devices have been cleared as prescription use devices for the following representative indications for use:

- For temporary placement during breast augmentation or reconstruction procedures to assist the surgeon in determining the appropriate size of the long-term breast implant

- For temporary insertion intraoperatively to evaluate the size and shape of the breast implant

- To evaluate the appropriate mammary prosthesis volume for each patient prior to implantation of mammary prosthesis

Regulatory History

- Mammary sizers are a pre-amendments 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 11 devices under the MRD product code.

Clinical Background

- The mammary sizer may be used in patients who are undergoing breast augmentation or reconstruction surgery.
- It is used to evaluate the appropriate mammary prostheses (i.e., breast implants) volume intraoperatively, before the prostheses are placed.
- The device is a tool used to aid in surgical decision making only during surgery.
- An alternative treatment option is to conduct the breast augmentation or reconstruction surgery without the use of a mammary sizer with the surgeon determining the breast implant size using their clinical judgement.

Literature Review

- A systematic literature review was conducted in an effort to gather any published information regarding the safety and effectiveness of mammary (breast implant) sizers under product code “MRD.”

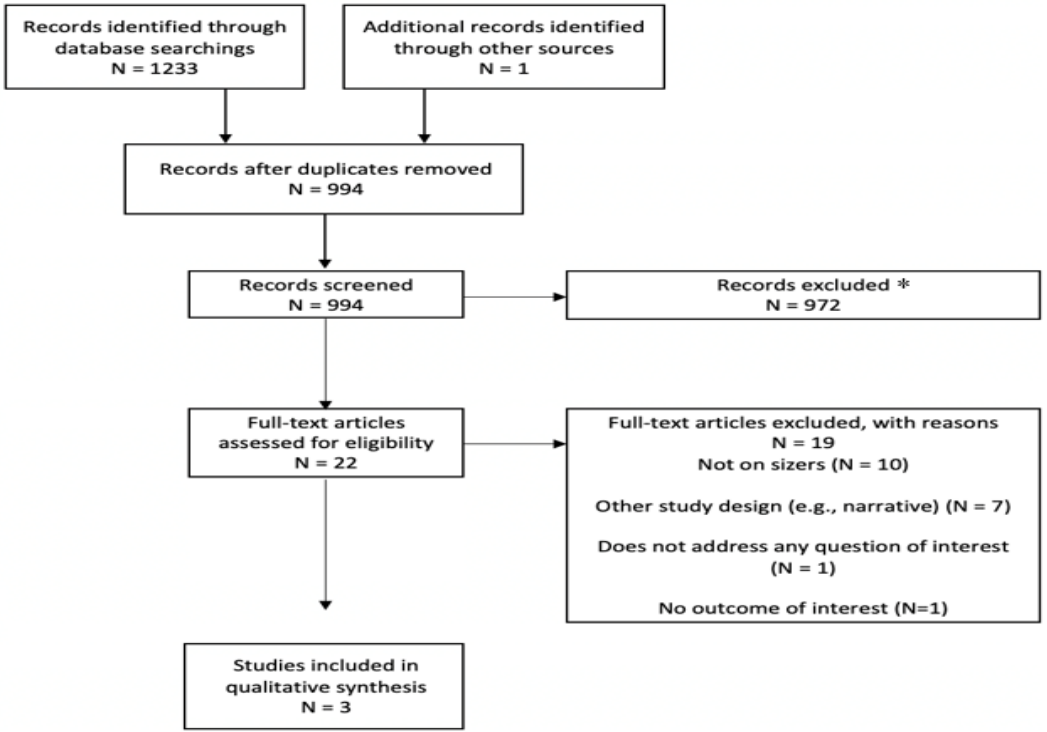
- Literature searches were conducted to identify any relevant articles published between April 1, 2012 and April 1, 2022.

- 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 1,234 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 22 literature references.

- A total of 3 published literature references, covering 3 retrospective studies, were determined to be relevant to the safety and/or effectiveness of breast implant sizers.



Literature Review – Safety Assessment

- Two articles did not report adverse events associated with mammary sizer use (Kim et al. and Wang et al.)

- One article (Khoo et al.) compared outcome of cases that used implant sizers versus those that did not
  - Breast implant sizer group had higher total complication rate when the permanent breast implant was placed compared to no mammary sizer
  - Limitation: if complication rates were truly based on mammary sizer use

Literature Review – Effectiveness Assessment

- Mammary sizers were used intraoperatively
- Articles in literature review did not describe overall effectiveness

Literature Review – Summation

- All three studies evaluated different outcomes associated with mammary sizer use.
- The reports evaluated:
  - comparison of complications amongst two groups of subjects to compare funnel use (Kim et al.)
  - the use of mammary sizers in nipple sparing mastectomies and reconstruction (Wang et al.)
  - mammary sizers in routine use compared to no use (Khoo et al.)

- The quality of evidence for the systematic literature review is low since only three studies met the search criteria, and all three studies evaluated different outcomes associated with mammary sizer use.

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 “MRD” (mammary sizer) with no date limitation through April 1, 2022:
  - The search resulted in the identification of 107 unique MDRs for inclusion in this analysis.
  - The 107 MDRs included 55 malfunctions and 52 serious injuries.

Medical Device Reports

Serious Injury	MDRs
Ruptured	19
Failed to remove sizer and exchange for breast implant	18
Foreign body on sizer	2
Systemic symptoms/Breast Implant Illness (BII) symptoms	2[a]
Capsular contracture	2[b]
Use of expired sizers	2
User error, damaged during use	2
Premature failure of the device	1
Defective device	1
No information available	1
Allergic reaction	1[c]
Burn to patient	1[d]

[a]One report identifies breast implant placed after mammary sizer use and one report does not provide any information

[b]Not enough information to determine if report is about mammary sizer left implanted or due to subsequent implant, such as breast implant

[c]Immediate reaction upon placing implant sizer, no further information provided

[d]Physician squeezed the sizer causing it to rupture and the “hot” gel inside to be pushed to the surface and burned the patient.

Medical Device Reports

Malfunction	MDRs
Ruptured	25
Foreign body on sizer	15
Greasy residue after sterilization	3
Failed to remove sizer and exchange with breast implant	3
Out of box failure (implant failed after opening package)	3
Use of expired sizers	2
User error, use of unsterile device	2[a]
Systemic symptoms/BII symptoms	1[b]
Use error, not following cleaning instructions	1

[a] Product was packaged in a way that led the user to believe it was sterile. One sizer reached the patient, the other was caught prior to implantation.

[b] Not enough information to know if report is about mammary sizers left in or subsequent implant, such as breast implant

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

- A review of the Medical Device Recall Database found four recalls for devices cleared for product code “MRD” (not time restricted):
  - One class III recall was initiated due to error in labeling, which resulted in barcodes on mammary sizers being unreadable by scanners
  - One class II recall was initiated due to expired mammary sizers being shipped to users
  - One class II recall was initiated due to certain mammary sizers that were packaged with the incorrect instructions for use
  - One class II recall was initiated due to error in labeling, which resulted in certain 380cc mammary sizers being labeled as 330cc mammary sizers

Risks

Identified Risk	Description/Examples
Adverse tissue reaction	Device material(s) may elicit adverse tissue reactions, such as allergic reaction, toxicity, and foreign body response.
Infection	Inadequate device sterilization or packaging integrity may lead to infection, leading to additional surgical procedures.
Device malfunction leading to increased operative time	Device malfunction may result in rupture, gel bleed, and gel migration leading to increased operative time and additional risks, such as increased anesthesia.
Use error/Improper device use	This can result from the device accidentally remaining implanted and not exchanged for a breast implant.

Risks and Mitigations

Identified Risk	Recommended Mitigation Measure
Adverse tissue reaction	Biocompatibility evaluation Labeling
Infection	Sterilization testing/validation/ information Reprocessing validation Shelf-life testing Labeling
Device malfunction leading to increased operative time	Non-clinical performance testing Labeling
Use error/Improper device use	Labeling

Proposed Classification

878.5060 Mammary sizer.

(a) *Identification.* A mammary sizer is 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.

(b) *Classification.*
Class II (special controls).

Proposed Special Controls

1. Non-clinical performance testing must demonstrate the 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 disinfection instructions for reusable devices.

Proposed Special Controls (cont'd)

6. Labeling must bear all information required for the safe and effective use of the device, specifically including the following:
   i) A clear description of the technological features of the device, including identification of device materials, shapes, and sizes.
   ii) Information on how the device operates.
   iii) Validated methods and instructions for reprocessing if the device is reusable, including the number of times device can be re-sterilized.
   iv) A warning against implantation of the device.
   v) A shelf life.
   vi) Disposal instructions.

U.S. FOOD & DRUG ADMINISTRATION

Thank You

Questions to Panel - MRD

Tajanay Ki, Lead Reviewer, OHT4

Question 1 to Panel

FDA has identified the following risks to health for mammary sizers:

Identified Risk	Description/Examples
Adverse tissue reaction	Device material(s) may elicit adverse tissue reactions, such as allergic reaction, toxicity, and foreign body response.
Infection	Inadequate device sterilization or packaging integrity may lead to infection leading to additional surgical procedures.
Device malfunction leading to increased operative time	Device malfunction may result in rupture, gel bleed, and gel migration leading to increased operative time and additional risks, such as increased anesthesia.
Use error/Improper device use	This can result from the device accidentally remaining implanted and not exchanged for a permanent breast implant.

Question 1 to Panel

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.

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 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.

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 2 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 mammary sizers cleared under product code “MRD”.

Question 2 to Panel

Following is a risk/mitigation table which outline the identified risks to health for this device type and the recommended controls to mitigate the identified risks.

Question 2 to Panel

Identified Risk	Recommended Mitigation Measure
Adverse tissue reaction	Biocompatibility evaluation Labeling
Infection	Sterilization testing/validation/information Reprocessing validation Shelf-life validation Labeling
Device malfunction leading to increased operative time	Non-clinical performance testing Labeling
Use error/Improper device use	Labeling

Question 2a to Panel

Please discuss whether the identified special controls for mammary sizers appropriately mitigate the identified risks to health and whether additional or different special controls are recommended.

Proposed Special Controls

1. Non-clinical performance testing must demonstrate the 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 disinfection instructions for reusable devices.
6. Labeling must bear all information required for the safe and effective use of the device, specifically including the following:
    i. A clear description of the technological features of the device, including identification of device materials, shapes, and sizes.
    ii. Information on how the device operates.
    iii. Validated methods and instructions for reprocessing if the device is reusable, including the number of times device can be re-sterilized.
    iv. A warning against implantation of the device.
    v. A shelf life.
    vi. Disposal instructions.

Question 3 to Panel

Please discuss whether you agree with FDA's proposed classification of Class II with special controls for mammary sizers. 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 “MRD”

Tajanay Ki, Lead Reviewer, OHT4