DE NOVO CLASSIFICATION REQUEST FOR
AEROFORM® TISSUE EXPANDER SYSTEM

REGULATORY INFORMATION

FDA identifies this generic type of device as:

> **Carbon dioxide gas controlled tissue expander**. A carbon dioxide gas controlled tissue expander is a prescription device intended for temporary subcutaneous or submuscular implantation to stretch the skin for surgical applications, specifically to develop surgical flaps and additional tissue coverage. The device is made of an inflatable elastomer shell and is filled with carbon dioxide gas. The device utilizes a remote controller to administer doses of carbon dioxide gas from an implanted canister inside the device.

NEW REGULATION NUMBER: 21 CFR 878.3510

CLASSIFICATION: CLASS II

PRODUCT CODE: PQN

BACKGROUND

DEVICE NAME: AeroForm® Tissue Expander System

SUBMISSION NUMBER: DEN150055

DATE OF DE NOVO: December 8, 2015

CONTACT: AirXpanders, Inc.
1047 Elwell Court
Palo Alto, CA 94303

INDICATIONS FOR USE

The AeroForm Tissue Expander System is used for soft tissue expansion in breast reconstruction following mastectomy, for the treatment of underdeveloped breasts, and for the treatment of soft tissue deformities in the breast.

The AeroForm Expander is intended for temporary subcutaneous or submuscular implantation and is not intended for use beyond six months.

LIMITATIONS

Prescription use only: Federal (USA) law restricts this device to sale by or on the order of a physician.

Limitations on device use are also achieved through the following statements included in the instructions for use:

Contraindications:

The AeroForm Tissue Expander System MUST NOT be used when:

- Magnetic Resonance Imaging (MRI) is required with the AeroForm Tissue Expander implanted. The AeroForm Tissue Expander is MR Unsafe. MRI equipment can cause movement of the expander and result in patient injury or expander displacement, requiring revision surgery.
- Tissue at the intended expansion site is determined unsuitable by the surgeon. To a varying degree, radiation damage, ulceration, compromised vascularity, history of compromised wound healing, infection, or scar deformity may affect tissue suitability.
- There is residual gross tumor at the intended expansion site.
- The patient has another electronic implant (e.g., pacemaker, defibrillator, or neurostimulator device).

Warnings:

Altitude Changes: The patient should not travel by air in a non-pressurized cabin while the Expander is implanted. The surgeon must approve flight travel for the patient, based on physical examination to determine if the patient's wound is adequately healed and they would tolerate the volume increase. (Refer to the labeling for additional information.)

Infection: DO NOT expose the Expander to contaminants that could increase the risk of infection. DO NOT implant in patients who present with an active infection, as this will increase the risk of peri-prosthetic infection.

Other Therapies: Diagnostic x-rays and diagnostic ultrasounds may be performed without affecting the Expander. DO NOT use shortwave diathermy, microwave diathermy or therapeutic ultrasound diathermy on patients implanted with an Expander. Energy from diathermy can be transferred to the Expander and can cause damage to the device.

Overfilling: DO NOT overfill the Expander. Excess volume cannot be removed without intentional rupture of the Expander. Therefore, use caution when filling the Expander to avoid overfilling. Please see labeling for additional information on overfilling.

Radiation Therapy: The decision to use radiation therapy should be made with the consultation of the radiation oncologist. Please see labeling for additional information on radiation therapy.

Sterility: DO NOT re-sterilize or re-use the Expander. The Expander is intended for single use only. Re-sterilization or re-use may impact device functionality or lead to

serious infection.

Temporary Device: DO NOT use the Expander for permanent implantation. The Expander is a temporary device intended for up to 6 months of implantation. Implantation longer than 6 months may lead to volume loss and depletion of CO_2 gas.

Precautions:

Avoid Contamination During Surgery: Surgeons must use aseptic technique to avoid contamination. DO NOT expose the tissue expander to lint, talc, sponge, towel and other contaminants. Contamination at the time of surgery increases the risk of peri-prosthetic infection, which could require premature removal of the tissue expander.

Avoid Damage During Surgery: Extreme care should be taken to avoid damage to the tissue expander during surgery. A sterile back-up Expander should be readily available at the time of surgery in case damage occurs. Expanders must be carefully inspected for nicks, tears, punctures or leaks prior to use. DO NOT alter the device. DO NOT attempt to repair damaged products.

Maintenance Dosing: Once the labeled volume is reached, a small amount of CO_2 will permeate from the Expander. To offset this permeation, patients must be instructed to "Maintenance Dose" to maintain the volume of the Expander. Failure to maintain the volume of the Expander may result in deflation and other potential complications. Refer to the "Manage Dosing" section of the labeling for additional details.

Surgical Planning: AirXpanders relies on the surgeon to know and follow proper surgical procedures specific to the expansion. Please see labeling for additional information on surgical planning.

PLEASE REFER TO THE LABELING FOR A MORE COMPLETE LIST OF WARNINGS, PRECAUTIONS AND CONTRAINDICATIONS.

DEVICE DESCRIPTION

The AeroForm® Tissue Expander System is comprised of the AeroForm Tissue Expander, the Dosage Controller, and the Physician Master Key (see Figure 1). Each system component is further explained in subsections below.

Figure 1: Image of AeroForm Tissue Expander System

AeroForm Tissue Expander

The AeroForm Tissue Expander is a sterile implant with an outer textured silicone shell and a non-distensible inner bag which are anatomically shaped to allow for directional expansion in the lower, anterior pole. The AeroForm Tissue Expander contains a reservoir of compressed carbon dioxide (CO_2), which is released within the AeroForm Tissue Expander by using the Dosage Controller. The outer shell has suture tabs to allow fixation of the device to the surrounding tissues to prevent rotation. A receiving antenna and electronics within the AeroForm Tissue Expander enable communication with the Dosage Controller. The AeroForm Tissue Expander has no intrinsic electrical power, batteries, or software, and can only be activated by the Dosage Controller. There are 3 different sizes of the expander, including small (400cc), medium (600cc), and large (850cc). The dimensions of the 3 different sizes of the AeroForm Tissue Expander are listed in Table 1 below:

Table 1: Available Models and Sizes of AeroForm Tissue Expander

Model #	Surface	Shape	Size	Width (cm) Un-inflated	Height (cm) Inflated	Projection (cm)	Volume (cc)
LP105-400	Textured	Anatomical	Small	12.5	11.0	8.0	400
LP120-650	Textured	Anatomical	Medium	14.0	12.5	9.5	600
LP130-850	Textured	Anatomical	Large	15.5	14.0	10.5	800

Dosage Controller

The Dosage Controller is a small, hand held battery-powered, non-sterile device. It activates the AeroForm Tissue Expander to release the programmed amount of CO_2 gas (10cc). The Dosage Controller is configured to provide coded instructions to its bonded AeroForm Tissue Expander. It has a single push button for ease of use and a bank of indicator lights (LEDs) and tones. The LEDs are bi-color, with amber and green lights, where green indicates successful communication and dosing and amber indicates a notification regarding communication, dosing or power down. Each dose administers 10cc of CO_2. There is a patient dosing limit of 3 (10cc) doses per day and a 3 hour time period between doses. A closer view of the Dosage Controller is provided in Figure 2 below.

Figure 2: Schematic of Dosage Controller

Physician Master Key

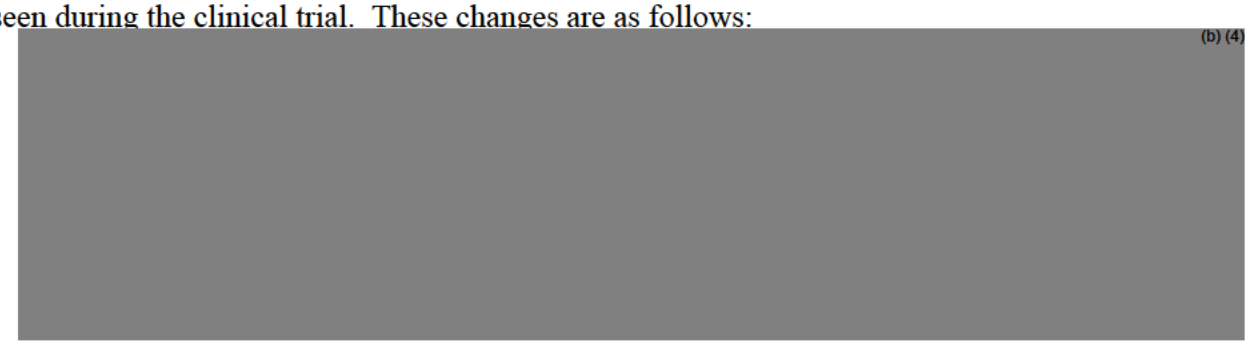
The Physician Master Key is used only by the physician in the operating room or in the physician office. With the Physician Master Key inserted into the Dosage Controller receptacle, the Dosage Controller can activate the Expander with no daily limit on the expansion volume. The Physician Master Key must remain plugged into the receptacle to continue functioning in this mode. Use of the Physician Master Key allows the physician to:

- Inflate the Expander intra-operatively to the desired intra-operative fill volume
- Add volume to the Expander at office visits, as therapeutically appropriate during the expansion process
- Add up to 25% of the labeled volume every 2 weeks (to maintain volume and adjust the volume based on CO_2 permeation).

The Physician Master Key is retained by the physician for use by the physician only, and is NOT provided to the patient. It will override the patient limits.

Modifications to the AeroForm Tissue Expander

At the start of the clinical trial, an earlier version of the device was initially used. This initial version of the AeroForm Tissue Expander was called the version 2.0 or V2.0. Modifications were made to the AeroForm Tissue Expander V2.0 in response to device malfunctions that were seen during the clinical trial. These changes are as follows:



When the above listed changes were made to the device, it was called the AeroForm Tissue Expander 2.5 or V2.5. Both the V2.0 and V2.5 devices were used in the clinical study. A justification was provided explaining how the data from the V2.0 devices are applicable to the final V2.5 devices. The changes did not affect the intended use of the device; rather they decreased malfunctions that were experienced with the previous version.

Please refer to the Instructions for Use, Patient Training Guide and Patient Home Instructions documents for additional details.

SUMMARY OF NONCLINICAL/BENCH STUDIES

BIOCOMPATIBILITY/MATERIALS

The AeroForm Dosage Controller, and Physician Master Key are expected to be limited superficial contact; therefore, they fall under the category of "surface devices", "skin", "limited" contact duration (≤24hrs), according to ISO 10993-1:2009 Biological evaluation of medical devices -- Part 1: Evaluation and testing within a risk management process. No biocompatibility testing was conducted on these components of the device.

The AeroForm Tissue Expander is implanted in breast tissue for > 30 days. It falls into the category of "Implant Devices, Tissue/Bone Communicating, permanent" contact duration (>30d) device according to ISO 10993-1:2009 Biological evaluation of medical devices -- Part 1: Evaluation and testing within a risk management process. Table 2 below summarizes the biocompatibility testing that was conducted on the AeroForm Tissue Expander.

Table 2: Biocompatibility testing conducted on AeroForm Tissue Expander

Biocompatibility Test	Acceptance Criteria	Results
Cytotoxicity (ISO MEM Elution)	The biological response of the test samples extract must be grade 2 (mild or less)	Pass
Sensitization (Maximization)	The test samples must show a grade of 1 or less when compared to the control	Pass

Biocompatibility Test	Acceptance Criteria	Results
Irritation (ISO Intracutaneous)	The difference between the mean score of the test samples and control groups, in terms of erythema and edema, must be less than 1.0	Pass
Acute Systemic Toxicity (USP Systemic Injection)	The test mice must not show a significantly greater reaction than the control mice	Pass
Acute Systemic Toxicity (USP Mediated Pyrogen)	The test rabbits must not show a temperature difference from the control of greater than or equal to 0.5°C	Pass
Sub-chronic toxicity	Evidence of irritation in the test animals will be scored and compared to the control animals	Pass
Chronic Toxicity	Evidence of irritation in the test animals will be scored and compared to the control animals	Pass
Genotoxicity (Bacterial Reverse Mutation)	The mean number of test revertants must be less than 2x the mean number of negative control revertants	Pass
Genotoxicity (Mouse Micronucleus)	The average % MN-RET for the test group must be less than 1.0%	Pass
Genotoxicity (Mouse Lymphoma)	The mutant frequency of the test sample must be 2X or less than that of the control	Pass
Implantation (2 week and 9 week)	The average macroscopic scores for test sample sites compared to control sites are correlated to a grade. The microscopic findings showing cellular changes will be graded according to severity (0-4) and any resulting irritant response indicated by a difference between test and control values will be graded as nonirritant, slight, moderate or severe.	Pass
Particulate Testing	Particle size [redacted] (b) (4) particles per mL Particle size [redacted] (b) (4) particles per mL (per EN45502-1)	Pass
LAL (Limulous Amoebocyte Lysate) Testing	Detected EU/device level is below [redacted] (b) (4) EU/device	Pass
Carcinogenicity	Analysis of the biological test results, chemical characterization data and literature review	Pass by analysis and risk assessment

SHELF LIFE/STERILITY

The AeroForm Tissue Expander is provided sterile. The Dosage Controller and Physician Master Key are provided non-sterile. The sterilization processes for the

AeroForm Tissue Expander include [redacted] (b) (4) and ethylene oxide per EN ISO 11135-1:2007. The AeroForm Tissue Expander is sterilized [redacted] (b) (4) (b) (4)

The AeroForm Tissue Expander is provided in an inner polyester (PETG) tray sealed with a Tyvek® lid. The sealed inner tray is placed into an outer PETG tray, which is sealed with a second Tyvek® lid. The double-sealed product tray is then placed into a sealed chipboard box. Multiple sealed and labeled chipboard boxes are placed in a shipper box for shipping and distribution.

The Dosage Controller package includes a sterile Aseptic Transfer pouch and the non-sterile Dosage Controller. Using standard sterility techniques, the Dosage Controller must be transferred to the Aseptic Transfer pouch in order to maintain sterility of the surgical field during the surgical procedure.

The shelf-life for the sterile AeroForm Tissue Expander is 12 months, based on accelerated and real time shelf-life studies. The test articles were environmentally conditioned based on ASTM D4332-2014 Standard Practice for Conditioning Containers, Packages, or Packaging Components for Testing, and EN 45502-1:1998, Clause 10.2 Active implantable medical devices; General requirements for safety, marking and information to be provided by the manufacturer. Following climatic conditioning, test articles were subjected to transit shipping and handling tests, as described in ASTM D4169-2014 Standard Practice for Performance Testing of Shipping Containers and Systems for packages up to 150 lbs. Test articles were then sealed in a pressure vessel and subjected to high pressure conditions, 150 kPa ± 5% for 1 hour (pressure is absolute) per EN 45502-1:1998, Clause 25.1. Package integrity and seal integrity were evaluated to ensure transportation and climactic conditioning did not impact the sterile barrier seal. Following testing and inspection of the product package and labeling, the product was then tested according to protocol to confirm performance and functionality after one year of real time storage. Performance testing included simulated use testing, functional testing, and shell integrity evaluation. After one year of both accelerated and real time aging, testing of the AeroForm Tissue Expander and its package met the requirements specified in the protocol, including packaging integrity and functional specifications. The testing supports the expiration date of 12 months and the AeroForm Tissue Expander is labeled with a 12 month shelf life.

The Dosage Controller has no expiration date. All Dosage Controller materials are rated for a shelf life of more than 10 years. The batteries have a minimum 10 year shelf life

based on analysis of the battery drain and the battery capacity.

ELECTROMAGNETIC COMPATIBILITY AND WIRELESS COEXISTENCE TESTING

Electromagnetic compatibility (EMC) testing was conducted on the device. The testing is summarized in Table 3 below:

Table 3: EMC and wireless coexistence testing conducted on the AeroForm Tissue Expander System

Test	Description	Standard	Result
Radiated emissions; transmitter spurious high	Place test article on 1m table in transmit mode, measure emission within 30MHz to 1000MHz range	EN 300 330-2: 2010-02 4.2.1.4 IEC 60601-1-2:2007	Pass
Limits for transmitters; transmitter spurious	Place test article on 1m table in transmit mode, measure emission in 9k to 30MHz range	EN 300 330-2: 2010-02 4.2.1.2 EN 300 330-2: 2010-02 4.2.1.4	Pass
Permitted frequency range of modulation bandwidth	Place test article on 1m table in transmit mode, measure emission within 13.56MHz ± 7kHz range	EN 300 330-2: 2010-02 4.2.1.1 EN 300 330-2:2010-02 4.2.1.4	Pass
Radiated immunity	Place test article in 3m chamber and subject to 3V/m radiation in 80-2500 MHz range	IEC 60601-1:2007	Pass
Magnetic immunity	Place test article inside coil and subject to 3A/m magnetic field, 3-axis	IEC 60601-1-2:2007	Pass
ESD	Hold ESD gun to target, apply 6kV contact discharge, 8kV air discharge. Repeat for 8kV contact discharge, 15kV air discharge	IEC 60601-1-2:2007	Pass
Immunity from hand held transmitters	Exposure of test articles to simulated handheld transmitter held in very close proximity to the device, to expose the device to very large electromagnetic fields	ANSI/AAMI PC69: 2007	Pass
Immunity from security and logistical systems	Exposure of test articles to devices intended to radiate large magnetic fields at or near the operating frequency of the AeroForm System	N/A	Pass

MAGNETIC RESONANCE (MR) COMPATIBILITY

The AeroForm Tissue Expander System is MR Unsafe. MRI equipment can cause movement of the Expander and result in patient injury or Expander displacement, requiring revision surgery.

SOFTWARE

Software for the device is consistent with a 'MAJOR level of concern', as discussed in the FDA document, "Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices," issued May 11, 2005.

Adequate documentation describing the software development program as required per the guidance document was provided and deemed adequate. Verification and validation (V & V) testing was conducted to address the potential hazards with satisfactory results. The software development procedures provide the foundation that the software will operate in a manner as described in the specifications.

An assessment of cybersecurity risks and mitigations was provided. The risks were identified as eavesdropping, man-in-the-middle attacks or data manipulation, communication data disruption, communication data corruption, and loss of information confidentiality, integrity, and availability. The mitigations included very near field communication, an active-passive communication mode, proprietary communication protocol between the controller and expander, serial number verification, and proprietary data key and data port.

The software documentation is in sufficient detail to provide reasonable assurance that the software performs as intended and all software-related risks have been adequately mitigated.

PERFORMANCE TESTING - BENCH

Additional bench testing is summarized in Table 4 below.

Table 4: Additional bench testing conducted on AeroForm Tissue Expander System

Test	Purpose	Acceptance Criteria	Results
Cycle Rub Test	The Cycle Rub Test simulates repeated severe flexing and delamination of the film barrier, representing the pectoral and serratus anterior muscles in the chest exerting compressive and shear forces on the Expander.	There are no major leaks or tears in the film or the seals, after 25,000 cycles.	The Expander successfully met the no leak and tear requirements after 25,000 cycles.
Impact Test	This test confirms the gas barrier and seal integrity by exerting a load resulting in 3.3 psi of internal pressure.	There are no ruptures after the impact test.	No ruptures were reported after the impact test.

Test	Purpose	Acceptance Criteria	Results
Impact Force Test	The purpose of this test is to characterize the effects of high impact loading on the CO2 reservoir and valve sub-assembly, and to assess the anticipated force that could damage the valve and/or forcefully dislodge the valve.	The device shall not fail or leak when experiencing forces less than 1700 lbs.	All acceptance criteria were met. The reservoir and valve assembly withstood an impact load of ~4X the human tolerance levels of 1700lbs without leakage. Impact loads to ~7X the human tolerance level resulted in slow leaks.
Leak Test	This test confirms that the tissue expander does not leak CO2 after all the simulated use tests have been completed.	The CO_2 concentration shall not increase more than 100 PPM.	The Expander successfully met the leak test requirements following functional testing.
Permeability Test	This test records the permeation rate after at least 10 days of a fully expanded Expander.	Small & Medium Size: Each test article shall have a daily average permeation rate of 0-4.1 mL CO_2 per day. Large Size: Each test article shall have a daily average permeation rate of 0-6.0 mL CO_2 per day.	The small and medium test articles met the daily average permeation rate of < 4.1 mL CO_2 per day. The large sample met the requirement for < 6.0 mL CO_2 per day.
Shell elongation	This test verifies that the Expander shell meets the tensile set as per ASTM F 1441-03, Section 9.2.2.1.	Maximum set shall be less than 10%.	All test articles passed the acceptance criteria.
Shell breaking force	This test verifies that the Expander shell meets the breaking force, as per ASTM F 1441-03, Section 9.2.2.2.	Ultimate breaking force in tension shall be no less than 2.5lbs.	All test articles passed the acceptance criteria.
Phone dial / shell joint test	This test verifies that the Expander shell meets the critical fused or adhered joints (Phone Dial / Shell joint test), as per ASTM F 1441-03, Section 9.2.8.1.	Adhered or fused joints or seams that are critical to the integrity of the device envelope shall not fail when the shell adjacent to the joint is stressed at 200% elongation for 10 seconds. Zero failures results in a minimum 95/90 Confidence/Reliability interval.	All samples passed the phone dial / shell joint seam test with no failures.

Test	Purpose	Acceptance Criteria	Results
Suture tab joint test	This test verifies that the strength of the Suture Tab to Shell joint, according to ASTM 1441-03, Section 9.2.8.1 (Critical Fused or Adhered Joints).	The joint shall not fail after being exposed to 200% elongation. Zero failures results in a minimum 95/90 Confidence/Reliability interval.	All samples remained fully intact, and achieved at least 200% elongation without any failures.
Suture tab tear strength	This test documents the tear strength on the Suture Tab component, according to ASTM 1441-03, Section 9.2.8.1 (Critical Fused or Adhered Joints).	The Suture Tab fixation hole shall withstand a tensile tear-out force of at least 2.5lb. Zero failures results in a minimum 95/90 Confidence/Reliability interval.	All suture tab fixation holes withstood a tensile tear-out force of at least 2.5lbs.

PERFORMANCE TESTING – ANIMAL

A sheep implant study was conducted for a preliminary safety evaluation prior to initiating the IDE clinical study. Twelve implants were surgically placed into two male ovine subjects (each animal had 6 expanders placed). All twelve tissue expanders responded to and communicated with their corresponding dosage controllers throughout the expansion period. The animals were monitored for signs of pain or discomfort. No adverse events were observed. The results of the sheep study showed that the device could be safely and effectively used *in vivo*.

SUMMARY OF CLINICAL INFORMATION

Report of Prior Investigations

A two-phase single center, prospective, open-label clinical study (PACE) was conducted in Perth, Australia. This study enrolled a total of 40 subjects in which 71 AeroForm Tissue Expanders were implanted. This includes 7 subjects (10 AeroForm Tissue Expander System version 1.0) in the PACE 1 Australia Feasibility Study and 33 subjects (61 AeroForm Tissue Expander System V2.0) in the PACE 2 Australia Feasibility Study. All devices expanded as intended and 100% of the Expanders were successfully exchanged to a permanent implant. The device performance and safety was verified in subjects enrolled in both phases of the study, demonstrating that the CO_2 based tissue expansion system could be used successfully and safely to expand breast tissue in patients undergoing two stage breast reconstruction.

In a second clinical study conducted in Australia, twenty-one (21) subjects were implanted with 34 AeroForm Expanders. The overall success rate was 94%, with no device-related reconstruction failures.

Pivotal Study

The XPAND trial (CPT-0003) was a pivotal, prospective, multi-center, randomized, controlled, open-label, study designed to compare the performance and safety of the AeroForm Tissue Expander System to currently legally marketed saline tissue expanders. Subjects satisfying the inclusion/exclusion criteria and agreeing to participate in the study were consented, enrolled and randomized to either the investigational arm (AeroForm Tissue Expander System) or the control

arm (standard saline tissue expander) using a 2:1 (AeroForm Tissue Expander System to saline) permuted block randomization process, stratified by investigational center and procedure (unilateral or bilateral). There were 17 investigational sites in the U.S. There were 158 subjects enrolled in the study with 106 subjects randomized to the investigational arm (AeroForm) and 52 subjects randomized to the control arm (Saline). There were 7 investigational subjects who were randomized to treatment, but did not receive the device. One investigational subject was randomized to treatment and a procedure was attempted; however, no device was implanted due to positive lymph nodes and radiation therapy was required. This patient was included in the evaluable numbers for the safety analysis, but not for the effectiveness analysis. A total of 151 patients (99 AeroForm patients and 52 saline patients) were evaluated.

Inclusion Criteria

1. Subject is female between the ages of 18-70.
2. Subject requires tissue expansion as part of breast reconstruction.
3. Subject is able and willing to comply with all of the study requirements
4. Subject has the physical, perceptual and cognitive capacity to understand and manage at-home dosing regimen

Exclusion Criteria

1. Subject's tissue integrity is unsuitable for tissue expansion
2. Subject has residual gross tumor at the intended expansion site
3. Subject has current or prior infection at the intended expansion site
4. Subject has clinically significant fibrosis due to previous radiation (except in the event that autologous tissue will be used).
5. Subject has planned radiation therapy at the intended expansion site during the time the expander is implanted.
6. Subject has a history of failed tissue expansion or breast implantation at the intended expansion site.
7. Subject has any co-morbid condition determined by the Investigator to place the subject at an increased risk of complications (e.g. severe collagen vascular disease, poorly managed diabetes).
8. Subject is taking any concomitant medications determined by the Investigator to place the subject at an increased risk of complications (e.g. prednisone, Coumadin).
9. Subject is currently participating in another investigational drug or device study.
10. Subject is current tobacco smoker.
11. Subject is obese (BMI > 33).
12. Subject is unwilling to comply with air travel or altitude restriction of not > 3300 feet (1000 meters) from baseline during the time the AeroForm Expander is implanted
13. Subject has currently implanted electronic device such as a pacemaker, defibrillator, neurostimulator device, or drug infusion device
14. Subject is pregnant or planning on becoming pregnant during the study period
15. Subject has a history of psychological condition, drug or alcohol misuse which may interfere with their ability to use the device safely

All subjects were followed by the investigator in the post-operative period. When their incisions were healed, they were ready to begin active expansion. Subjects in the investigational arm were

given the Dosage Controller to expand at home with up to three (10cc) doses per day based on their comfort level. Subjects in the saline expander arm were injected with a bolus of saline through the magnetic port on the outer surface of the expander. These subjects received periodic bolus saline injections during their follow up visits to fill their expanders. The investigator determined the amount of saline to be added to the saline expander arm based on patient tolerance and need. All subjects were followed weekly until expansion was complete and monthly thereafter, until their procedure was scheduled to remove the expander(s) and to place permanent breast implant(s).

The timing of the exchange procedure was at the discretion of the investigator and needs of the subject. The subject's participation in the study was complete when their expander(s) were removed. Follow-up was discontinued if the subject was terminated or voluntarily withdrew from the study.

Primary Endpoint

The performance of the device was evaluated by successful tissue expansion and exchange to a permanent breast implant unless precluded by a non-device related event. The primary endpoint was analyzed per breast. Breasts in which the expander was removed and/or replaced due to a device related adverse event or a device malfunction were counted as failures.

The overall study success was based on an expected treatment success rate of 95%, with a -10% margin of non-inferiority when compared to the saline control group.

Secondary Effectiveness Endpoints

The usability of the device was evaluated by:

1. The average number of days to achieve the desired expansion (onset of active expansion to completion of expansion)
2. The average number of days for completion of stage 1 reconstruction (expander implantation to permanent implant exchange).
3. Subject reported pain ratings during active expansion
4. Overall subject satisfaction
5. Overall physician satisfaction

Safety Endpoints

The safety of the device was evaluated by:

1. Device related adverse events
2. Serious device related adverse events
3. All adverse events, regardless of whether serious or there is a causal relationship to the device.
4. All serious adverse events, regardless of whether there is a causal relationship to the device.
5. Device failures leading to expander removal and/or replacement.

Randomization

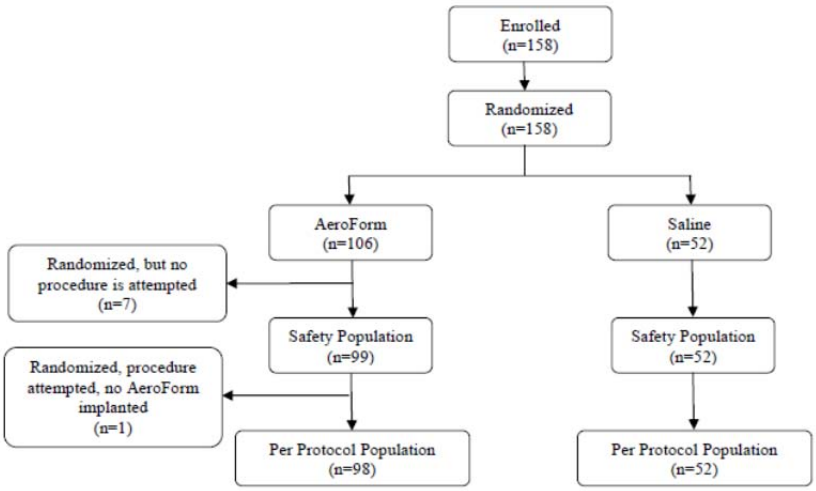
Subjects were randomized to either the investigational arm (AeroForm Tissue Expander System), or the control arm (standard saline tissue expander) using a 2:1 (AeroForm Tissue Expander System to saline) permuted block randomization process, stratified by investigational center and

procedure (unilateral or bilateral). A computerized system was used to generate the randomization scheme to assign the subject to the control arm or the investigational arm. The randomization was stratified per investigational site and procedure (unilateral or bilateral) to ensure the same number of saline and AeroForm tissue expanders per site. The same type of expander was placed on each side in subject's having a bilateral procedure.

Subject Enrollment

One hundred and fifty-eight (158) subjects were enrolled from 11/11/2011 through 12/23/2014 at 17 U.S. investigational sites. Subjects were randomized (2:1) to the investigational arm (AeroForm) (n=106) or the control arm (Saline) (n=52). All enrolled subjects were assigned to analysis cohorts as defined in the statistical analysis plan. There were 7 investigational subjects who were randomized to treatment, but did not receive the device. One investigational subject was randomized to treatment and a procedure was attempted, however no device was implanted due to positive lymph nodes and radiation therapy was required. This patient was included in the evaluable numbers for the safety analysis, but not for the effectiveness analysis. A total of 151 patients (99 AeroForm patients and 52 saline patients) were evaluated. The patient disposition is shown in Figure 3 below:

Figure 3: Patient Disposition



There were 98 subjects who received the AeroForm device in the investigational arm. Of the 98 AeroForm subjects, 54 patients received the V2.0 Expander and 44 patients received the V2.5 Expander (90 breasts received V2.0 and 78 breasts received V2.5).

No subjects were lost to follow up. Ninety-eight (98%, 147/150) of the implanted subjects completed the study. Three implanted subjects did not complete the study and were considered failures. This includes 2 subjects in the AeroForm arm and 1 subject in the saline arm. The first subject in the AeroForm arm who did not complete the study had bilateral expanders and experienced unilateral under-expansion. The subject elected to have only fat grafting, not to complete reconstruction and had both expanders removed, with no permanent implants placed. The second subject in the AeroForm arm who did not complete the study had bilateral expanders and experienced unilateral deflation. The subject elected to have both expanders removed and replaced with saline expanders and complete reconstruction at a later time. The subject in the

control arm who did not complete the study had bilateral expanders and experienced unilateral exposure. The subject elected to have both saline expanders removed, not to complete reconstruction, and had no permanent implants placed.

Primary Endpoint Data

The Treatment Success Rate per breast (excluding non-device related failures) for AeroForm is 96.1% (149/155). The Treatment Success Rate per breast for Saline is 98.8% (82/83). The difference in the treatment success rate (AeroForm - Saline) is -2.7% with a lower confidence limit of -7.3%, meeting the non-inferiority margin of > -10%.

Secondary Endpoints Data

The median number of days to complete expansion, and similarly, the median number of days for completion of reconstruction were reduced in the AeroForm group compared to the saline group. The median days to complete expansion was 21.0 (95% CI 15.0, 24.0) days for AeroForm and 46.0 (95% CI 38.0, 55.0) days for saline. The median days to complete breast reconstruction was 108.5 (95% CI 99.0, 117.0) days for AeroForm and 136.5 (95% CI 119.0, 147.0) days for saline.

Pain assessment is a patient reported outcome score and was judged using an 11-point visual analog scale with higher numbers representing higher levels of pain. The results show no difference in the intensity of the pain reported by patients implanted with the AeroForm device or the saline expander at the first visit after Start of Expansion (Average = 2.2 AeroForm, 1.9 saline) or for the worst pain experienced overall (Average = 4.5 AeroForm, 4.6 saline).

Overall, subjects were satisfied with the expansion process in 78% of the reconstructions with AeroForm and 91% with Saline. Analyzing the data for v2.5 only (n=69), 84% of the responses were mildly, moderately, or very satisfied.

Physician satisfaction with the results of expansion was 68% with AeroForm, and 92% with Saline. The lower satisfaction scores observed with the AeroForm were a direct reflection of the device malfunctions and gradual loss of volume that were experienced with the V2.0 device, which was used at the beginning of the clinical trial. Dissatisfaction comments were primarily related to permeation (loss of volume), bulkiness of the device, and physician modes. The satisfaction scores improved with V2.5 after the introduction of the enhanced inner liner which reduced permeation, as well as the software reprogramming to increase the capability of the physician to adjust the volume. Analysis of device V2.5 data alone resulted in physician satisfaction of 83% with the expansion results.

Safety

The number of subjects with any adverse event was 63 (63.3%) for the AeroForm arm and 33 (63.5%) for the Saline arm. The number of subjects with any adverse event related to the study device was 21 (21.2%) for the AeroForm Arm and 10 (19.2%) for the Saline arm. The number of subjects with any adverse event related to the study procedure was 46 (46.5%) for the AeroForm arm and 24 (46.2%) for the Saline arm. The proportion of subjects with any adverse event, any device-related adverse event and any procedure-related adverse event was similar between treatment groups. In addition, the treatment groups were, in general, similar in the

incidence of specific breast-related adverse events. There were 53 subjects (53.5%) in the AeroForm arm and 23 subjects (44.2%) subjects in the Saline arm who experienced breast related adverse events. The breast related adverse events that are most relevant to the study and device are listed in Table 5 below:

Table 5: Breast Related Adverse Events Observed in Pivotal Study

	AeroForm		Saline	
	Breasts (n=169) Quantity (%)	Subjects (n=99) Quantity (%)	Breasts (n=88) Quantity (%)	Subjects (n=52) Quantity (%)
Breast Related AEs*	74 (43.8%)	53 (53.5%)	35 (39.8%)	23 (44.2%)
Allergic/Foreign Body Reaction	0 (0%)	0 (0%)	2 (2.3%)	1 (1.9%)
Bleeding, Post Procedure	1 (0.6%)	1 (1.0%)	0 (0%)	0 (0%)
Capsular Contracture	1 (0.6%)	1 (1.0)	0 (0%)	0 (0%)
Device Displacement	0 (0%)	0 (0%)	3 (3.4%)	2 (3.8%)
Device Malfunction	7 (4.1%)	6 (6.1%)	1 (1.1%)	1 (1.9%)
Extrusion	2 (1.2%)	1 (1.2%)	1 (1.1%)	1 (1.9%)
Hematoma	2 (1.2%)	2 (2.0%)	3 (3.4%)	3 (5.8%)
Infection	9 (5.3%)	8 (8.1%)	6 (6.8%)	5 (9.6%)
Inflammation	15 (8.9%)	12 (12.1%)	5 (5.7%)	4 (7.7%)
Delayed Wound Healing, Tissue Necrosis	16 (9.5%)	11 (11.1%)	4 (4.5%)	3 (5.8%)
Procedural Pain	10 (5.9%)	7 (7.1%)	10 (11.4%)	7 (13.5%)
Seroma	15 (8.9%)	11 (11.1%)	5 (5.7%)	4 (7.7%)
Wound Dehiscence	2 (1.2%)	2 (2.0%)	1 (1.1%)	1 (1.9%)

*Adverse events coded using the MedDRA dictionary v18.0. The tables include counts and percentages. At each level of summation, breasts are counted only once.

Table 6 below lists the adverse events for the AeroForm investigational arm divided by the different versions of the device (Version 2.0 and Version 2.5).

Table 6: Breast Related Adverse Events Observed in Version 2.0 and Version 2.5 of AeroForm Expanders

	Breasts Receiving AeroForm Expander Version 2.0 N=90 n (n/N%)	Breasts Receiving AeroForm Expander Version 2.5 N=78 n (n/N%)
Breast Related AEs*	52 (57.8%)	22 (28.2%)
Post-Operative Wound Complication (Necrosis)	13 (14.4%)	3 (3.8%)
Seroma	4 (4.4%)	11 (14.1%)
Hematoma	1 (1.1%)	1 (1.3%)
Post-Operative Wound Infection	8 (8.9%)	1 (1.3%)
Wound Dehiscence	2 (2.2%)	0 (0.0%)
Extrusion	1 (1.1%)	1 (1.3%)
Capsular Contracture	1 (0.6%)	0 (0%)
Procedural Pain	8 (8.9%)	2 (2.6%)
Device Malfunction	5 (5.6%)	2 (2.6%)
Device Dislocation	0 (0%)	0 (0.0%)
Foreign Body Reaction	0 (0%)	2 (0.0%)

*Adverse events coded using the MedDRA dictionary v18.0. The tables include counts and percentages. At each level of summation, breasts are counted only once.

Device Malfunctions

Communication failures were reported for 9 (5.4%) AeroForm expanders used in the study; all failures were observed with V2.0 devices. Failure to reach or maintain volume, or the incidence of deflation of the device, was reported for 42 (46.7%) V2.0 devices. The device was modified

to mitigate this issue. The design changes of the V2.5 devices reduced this mode of device failure to 12 incidences, or from 46.7% to 15.4%.

Five (5) devices over-expanded due to failure of the micro valve to seal properly and required deflation of the expanders using a hypodermic needle. A needle puncture compromises the integrity of the device and device explantation is necessary.

All device malfunctions are listed in Table 7 below:

Table 7: Device Malfunctions Experienced in AeroForm Expanders

Event Description	AeroForm V2.0 n=90	AeroForm V 2.5 n=78	All AeroForm n=168
Loss of Communication	9 (10%)	0 (0%)	9 (5.4%)
Under Expansion/Deflation (Total)	42 (46.7%)	12 (15.4%)	54 (32.1%)
Under-Expansion – Failure to Reach Full Volume	1 (1.1%)	2 (2.6%)	3 (1.8%)
Deflation – Failure to Maintain Volume	16 (17.8%)	1 (1.3%)	17 (10.1%)
Deflation – Gradual	23 (25.6%)	8 (10.3%)	31 (18.5%)
Deflation – Sudden	2 (2.2%)	1 (1.3%)	3 (1.8%)
Over-Expansion	4 (4.4%)	1 (1.3%)	5 (3.0%)
Rupture	0 (0%)	0 (0%)	0 (0%)

As shown in Table 6, there were 7 AeroForm device malfunctions that led to breast related adverse events, or more specifically those patients that had a failed reconstruction due to the device related failure. This includes 5 cases of over-expansion, 1 case of deflation and 1 case of under expansion.

Carbon Dioxide Permeation

At the start of the clinical trial, a different version of the device was used, V2.0. With the V2.0, there were many reports of carbon dioxide permeating or leaking through the shell. This reported leakage did not result in abnormal tissue responses or clinical chemistry responses. There were, however, noticeable volume losses noted in the expanders. In the device malfunctions data (Table 7), this is categorized as either under expansion or deflation. With the original version V2.0, there were 42 instances of under expansion/deflation. The sponsor modified the design on their device, as described in the "Modifications to the AeroForm Tissue Expander" section of this document. As explained, an additional layer was added to the inner bag to increase durability and decrease permeation of carbon dioxide. In addition, a physician mode was added to allow the capability of adding 25% of full volume every two weeks. Once all the device modifications were implemented, the device (known as V2.5) showed a reduced number of 12 instances under expansion/deflation.

When expansion is complete and the labeled volume is reached, a small amount of CO_2 may permeate from the Expander. To offset this permeation, subjects will need to administer a maintenance dose. The maintenance dosing allows subjects to administer enough doses to account for the small amount of carbon dioxide that can permeate from the expander. Maintenance dosing is required to maintain the volume and prevent deflation.

Continued Access Study

When enrollment was complete for the pivotal study, patients continued to be enrolled under the Continued Access Study (CAS) IDE provision. XPAND II CAS is a prospective, multi-center, single arm study of the V2.5 device. As of June 8, 2016, a total of 28 subjects (49 breasts) have been treated at 6 clinical sites. Eleven (11) subjects (21 breasts) have completed the final study visit and complete data are available. An additional 4 subjects (6 breasts) have undergone the explant procedure but only have partial data available as they have not completed their final study visits.

The primary endpoint of Treatment Success in the XPAND II CAS was 100% (n=18 breasts). Two patients had their devices (3 expanders) removed for non-device related reasons. The first subject elected to have both expanders removed due to severe reactions to multiple antibiotics and withdrew from the study. The second subject had an incision which failed to heal properly and led to an open wound, requiring removal of her left expander and replacement with a saline expander. Expansion was completed and both tissue expanders were exchanged to breast implants.

The secondary endpoints, pain and satisfaction, were assessed. Pain was assessed at two time points: at the start of expansion and at the first visit after start of expansion. At the start of expansion, average pain was reported as 1.8 in 24 subjects with data available, and 2.3 in 26 subjects with data available for the first visit after the start of expansion. Satisfaction data from both subject and physician surveys in XPAND II are available for subjects who have completed their final study visit (n=11). Two patients and one physician did not complete the XPAND II survey. Overall, 89% (8/9) subjects and 90% (9/10) physicians were satisfied with the device performance and 80% (8/10) physicians were satisfied with the results of expansion.

Dissatisfaction comments were primarily related to permeation and bulkiness of the device. One physician was neither satisfied nor dissatisfied and one patient and their physician were moderately dissatisfied due to gradual volume loss, requiring office dosing.

There were 5 breast-related adverse events reported in the CAS. Those events most relevant to the study are summarized in Table 8 below.

Table 8: Breast Related Adverse Events Observed in XPAND II CAS

	Breasts (n=21) Quantity (%)	Subjects (n=11) Quantity (%)
Breast Related AEs*	5 (23.8%)	4 (36.4%)
Inflammation	1 (4.8%)	1 (9.1%)
Post-Operative Wound Infection	1 4.8%)	1 (9.1%)
Wound Dehiscence	1 (4.8%)	1 (9.1%)

*Adverse events coded using the MedDRA dictionary v18.0. The tables include counts and percentages. At each level of summation, breasts are counted only once.

There was one instance of loss of volume which was managed by the surgeon with office dosing, leading to a successful exchange procedure. There were no new failure modes identified and no over-expansion or sudden deflations occurred in the XPAND II study.

HUMAN FACTORS

Human factors evaluation and validation was performed in compliance with ANSI/AAMI HE 75:2009, *Human factors engineering—Design of medical devices*, and EN 62366-2008 Medical devices - Application of usability engineering to medical devices. A Formative Human Factors Usability study was performed to optimize the design of the Dosage Controller, followed by a Summative Human Factors Validation study. These studies were performed to assure that design of the Dosage Controller and patient instructions are easily understood by the intended user population.

The study results, analyses and conclusions established that the AeroForm Tissue Expander System is safe and effective for the intended users, its intended uses, and use environments.

LABELING

Labeling has been provided which includes the instructions for use and an appropriate prescription statement as required by 21 CFR 801.109.

Device-specific risks addressed in the labeling include:

- Patients must not undergo Magnetic Resonance Imaging (MRI) while the AeroForm Tissue Expander is in place. MRI equipment can cause damage to the electronics and/or result in movement or displacement of the Expander that could lead to patient injury or revision surgery.

- During the ascent on commercial flights, the AeroForm Tissue Expander will increase in volume. An increase in volume may cause the patient discomfort and the possibility of pressure related wound complications. The Expander volume will return to its original state and the filling sensation that the patient may experience will subside when the plane descends and lands. The surgeon must approve flight travel for the patient, based on physical examination to determine if the patient's wound is adequately healed and if the patient would tolerate the volume increase. Depending on the size and how full the AeroForm Tissue Expander is, the patient will experience an average volume increase during air travel as follows:

Percent Full*	**20%**	**40%**	**60%**	**80%**	**100%**
Small (400cc)	44cc	59cc	75cc	87cc	96cc
Medium (600cc)	61cc	88cc	115cc	131cc	141cc
Large (800cc)	83cc	122cc	160cc	164cc	143cc

*Percent full as indicated by lighting bank on Controller

For moderate altitude change, such as during car travel, if increasing pressure and discomfort in the breast is experienced, the patient should stop the ascent and wait for the discomfort to pass. If the discomfort does not pass, the patient should return to lower altitude. The AeroForm Tissue Expander has not been evaluated in other pressurized environments (i.e., scuba diving, or hyperbaric chambers). The patient should not travel by air in a non-pressurized cabin while the Expander is implanted.

- The ability to establish communication between the Expander and the Controller may be impaired by electromagnetic interference from other RF wireless devices operating nearby. Interference from other RF wireless devices may be resolved by simply moving away from the other RF wireless device.

Physician labeling includes instructions for use by the physician and includes the following information:

- Device description and indications for use.
- Instructions for use including information that should be provided to the patient.
- Contraindications, warnings, precautions, and limitations for safe use of the device and adverse events associated with device use.
- Information on how the device operates including dosing instructions, dosing limits and the physician fill mode.
- A description of the verified temperature controls and safety features included in the device.
- A summary of the pivotal clinical investigation information.

Additional labeling information for the physician includes a Physician Quick Reference Card.

Patient labeling (patient guide) includes instructions for the patient and includes the following information:

- Contraindications, warnings, and precautions.
- Description of the device and device care.
- Risks associated with device use.
- Explanation of breast reconstruction and breast reconstruction with the device, including alternative treatments.
- Instructions for dosing and an explanation of dosage controller notifications.
- Summary of clinical investigational information.
- Glossary of terms.

Additional patient labeling information includes a patient reference card and a patient ID card, which includes information on metal detectors.

Presentations to guide the physician and patient in the proper use of the device have been prepared. The "physician training presentation for medical professionals" is used to explain the device to medical personnel. The "patient training presentation" is a presentation that is to be used by the physician to explain the device to the patients.

After the patient receives training, they must demonstrate comprehension of the device or they should be re-trained.

RISKS TO HEALTH

Table 9 below identifies the risks to health that may be associated with use of a carbon dioxide gas controlled tissue expander and the measures that have been used to mitigate these risks.

Table 9: Identified Risks and Mitigation Measures

Identified Risk	Mitigation Measure
Pain • From Overexpansion with Carbon Dioxide	• Labeling • Software verification, validation and hazard analysis
Tissue Damage • From Overexpansion with Carbon Dioxide	• *In-vivo* performance testing • Labeling • Software verification, validation and hazard analysis
Prolonged Treatment Time • Due To Under Expansion Because of Carbon Dioxide Permeation • Due to Overexpansion with Carbon Dioxide	• *In-vivo* performance testing • Non-clinical performance testing • Labeling • Software verification, validation and hazard analysis

Re-operation • Due to No Expansion Because of Device Failure • Due to Overexpansion with Carbon Dioxide	• *In-vivo* performance testing • Non-clinical performance testing
Underexpansion, Overexpansion, or No Expansion • Due To Interference With Other Devices • Due to Use Error	• Electromagnetic compatibility, electrical safety, and wireless compatibility testing • Labeling • Software verification, validation and hazard analysis • Human factors testing • Patient training
Adverse Tissue Reaction	• Biocompatibility evaluation
Infection	• Sterilization validation • Shelf life testing

SPECIAL CONTROLS:

In combination with the general controls of the FD&C Act, the carbon dioxide gas controlled tissue expander is subject to the following special controls:

1. *In-vivo* performance testing must be conducted to obtain the adverse event profile associated with use, and demonstrate that the device performs as intended under anticipated conditions of use
2. The patient-contacting components of the device must be demonstrated to be biocompatible
3. Performance data must demonstrate the sterility of patient-contacting components of the device
4. 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. Cycle testing of expander showing that there are no leaks or tears after repeated cycling
    b. Mechanical assessment of implanted CO_2 canister including high impact testing
    c. Leak testing of expander showing that device does not leak CO_2
    d. Assessment of gas permeability during expansion and after full expansion
    e. Mechanical assessment of expander (tensile set, breaking force, shell joint test, and fused or adhered joint testing)
5. Performance data must be provided to demonstrate the electromagnetic compatibility, electrical safety, and wireless compatibility of the device
6. Software verification, validation and hazard analysis must be performed

7. Performance data must support shelf life by demonstrating continued sterility of the device or the sterile components, package integrity, and device functionality over the identified shelf life
8. Human factors testing and analysis must validate that the device design and labeling are sufficient for the end user
9. Physician labeling must include:
    a. The operating parameters, name, and model number of the indicated external dosage controller
    b. Information on how the device operates and the typical course of treatment
    c. Information on the population for which the device has been demonstrated to be effective
    d. A detailed summary of the device technical parameters
    e. Provisions for choosing an appropriate size implant that would be exchanged for the tissue expander
10. Patient labeling must include:
    a. Warnings, precautions, and contraindications, and adverse events/complications
    b. Information on how the device operates and the typical course of treatment
    c. The probable risks and benefits associated with the use of the device
    d. Post-operative care instructions
    e. Alternative treatments
11. Patient training must include instructions for device use, when it may be necessary to contact a physician, and cautionary measures to take when the device is implanted.

BENEFIT/RISK DETERMINATION

The risks of the AeroForm Tissue Expander System are based on nonclinical laboratory and/or animal studies as well as data collected in a clinical study described above. In summary, the risks associated with use of the device include pain from overexpansion with carbon dioxide, tissue damage from overexpansion with carbon dioxide, prolonged treatment time due to under expansion because of carbon dioxide permeation, re-operation due to no expansion because of device failure, under or no expansion due to interference with other devices, adverse tissue reaction, infection, allergic/foreign body reaction, under or overexpansion of device from user error, capsular contracture, device displacement, extrusion, hematoma, delated wound healing/ tissue necrosis, seroma, wound dehiscence, premature expander removal, rupture, device malfunction, and deflation. There were 53 subjects (53.5%) in the AeroForm arm and 23 subjects (44.2%) subjects in the Saline arm who experienced breast related adverse events. The breast related adverse events that are most relevant to the study and device are listed in Table 10.

Table 10: Breast Related Adverse Events (most relevant to the study)

Event	Incidence
Post-Operative Wound Complication (Necrosis)	9.5%
Seroma	8.9%
Hematoma	1.2%
Post-Operative Wound Infection	5.3%

Event	Incidence
Wound Dehiscence	1.2%
Extrusion	1.2%
Capsular Contracture	0.6%
Procedural Pain	5.9%
Device Malfunction	4.1%

Device malfunctions seen in the AeroForm breasts are listed in Table 11:

Table 11: Device Malfunctions

Malfunction	Incidence
Loss of Communication	5.4%
Under Expansion/Deflation (Total)	32%
Under-Expansion – Failure to Reach Full Volume	1.8%
Deflation – Failure to Maintain Volume	10.1%
Deflation – Gradual	18.5%
Deflation – Sudden	1.8%
Over-Expansion	3%

The probable benefits of the AeroForm Tissue Expander System are also based on nonclinical laboratory and animal studies as well as on data collected in the clinical studies as described above. The benefits of the study included a reduction in the median number of days to complete expansion, and the median number of days for completion of reconstruction. Patients can benefit from the device by the need for fewer office visits to the surgeon for expansion, avoidance of needle puncture for expansion, and faster time to completion of expansion and reconstruction. Overall, subjects were satisfied with the expansion process in 78% of the reconstructions with AeroForm and 91% with Saline. Analyzing the data for V2.5 only (n=69), 84% of the responses were satisfied.

Additional factors to be considered in determining probable risks and benefits for the AeroForm Tissue Expander System include noting that the clinical study design was robust. The study was prospective, randomized and controlled. There was no loss to follow-up and low missing data. There were no major deviations from the study protocol. There is a Continued Access Study that has data that supports the study robustness. There were limitations to the study, including a modification of the device made during the study resulted in a smaller number of subjects that received the final device (44/98); the evaluators were non-blinded and therefore aware of which device was placed; and the largest size of the expander was under represented in its utilization in the study, however, this limitation was observed in both the saline and AeroForm arms. Despite the limitations, the study design remains robust. In addition, 3 OUS clinical studies were performed to demonstrate the safety and effectiveness of the AeroForm System.

Patient Perspectives

Patient perspectives considered for the AeroForm® Tissue Expander System included:

- Subject reported pain ratings during active expansion.
- Overall subject satisfaction.
- A human factors evaluation whereby the patients assessed the patient instructions to assure that they were easily understood.
- A patient training process, whereby after receiving training, the patient will be assessed regarding their understanding.
- Patient has control over expansion process.

Benefit/Risk Conclusion

In conclusion, given the available information above, the data support that for soft tissue expansion in breast reconstruction following mastectomy, treatment of underdeveloped breasts, and treatment of soft tissue deformities for a time period not extending beyond six months, the probable benefits outweigh the probable risks for the AeroForm Tissue Expander System. The device provides substantial benefits and the risks can be mitigated by the use of general and the identified special controls.

CONCLUSION

The De Novo request for the AeroForm® Tissue Expander System is granted and the device is classified under the following:

Product Code: PQN
Device Type: Carbon dioxide gas controlled tissue expander
Class: II
Regulation: 21 CFR 878.3510