# SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

## I. GENERAL INFORMATION

| | |
|---|---|
| Device Generic Name: | Saline-Filled Breast Implant |
| Device Trade Name: | IDEAL IMPLANT® Saline-filled Breast Implant |
| Device Procode: | FWM |
| Applicant's Name and Address: | Ideal Implant Incorporated<br>5005 LBJ Freeway<br>Suite 900<br>Dallas, TX 75244 |
| Date(s) of Panel Recommendation: | None |
| Premarket Approval Application (PMA) Number: | P120011 |
| Date of FDA Notice of Approval: | November 14, 2014 |

## II. INDICATIONS FOR USE

The IDEAL IMPLANT Saline-filled implants are indicated for women at least 18 years old undergoing:

- **Primary breast augmentation** to increase breast size.
- **Revision breast augmentation** to correct or improve the result of a primary breast augmentation surgery.

## III. CONTRAINDICATIONS

Breast implant surgery should not be performed in:

- Women with existing cancer or pre-cancer of their breast who have not received adequate treatment for those conditions.
- Women with active infection anywhere in their body.
- Women who are currently pregnant or nursing.

## IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the Ideal Implant Saline-filled breast implant labeling.

The IDEAL IMPLANT has not been studied for use in breast reconstruction and therefore is not indicated for primary breast reconstruction, revision breast reconstruction, or if there will be radiation of the breast.

## V. DEVICE DESCRIPTION

The IDEAL IMPLANT is a round, smooth-surface, saline-filled breast implant that is supplied sterile in a dual tray packaging system with two disposable fill tubes and reflux valves. It was developed to provide women and surgeons with another option in addition to the current saline-filled implants or silicone gel-filled implants.

While the currently available, FDA-approved saline-filled implants have a single lumen within a single shell made from cross-linked silicone elastomer, the IDEAL IMPLANT has two lumens within two nested shells that are attached at the patch on the back of the implant. The inner lumen within the inner shell is filled through a valve in the patch. The outer lumen within the outer shell and surrounding the inner shell is filled through a valve on the front. Unattached and floating within the outer lumen is a baffle structure designed to restrict movement of the saline in the outer lumen. Table 1 below shows that the amount of material required for the baffle structure is proportionate to the size of the implant and the fill volume in the outer lumen. This baffle structure is comprised of one to three nested baffle shells that are perforated with slits so the saline is free to move through the slits, as well as around and between the shells. Each baffle shell is made of the same acetoxy-cure, room temperature vulcanized (RTV) silicone material as the inner and out shells. For each size implant, the inner lumen is filled with a set volume of saline and the outer lumen is filled with a volume of saline, selected by the surgeon from the range shown in Table 1 ("High" to "100%") to achieve the desired Total Implant volume. The implant may be filled before or after it has been placed in a submuscular or subglandular pocket. Figure 1 shows a cut-away drawing of an IDEAL IMPLANT (335 cc to 555 cc size) showing the inner shell, the outer shell, the baffle structure floating in the outer lumen comprised of two baffle shells perforated with slits, the valve in the patch to fill the inner lumen and the valve on the front to fill the outer lumen. (The methods of cure/vulcanization for the shells, valve, patch, and valve-strap are summarized in Table 3.)

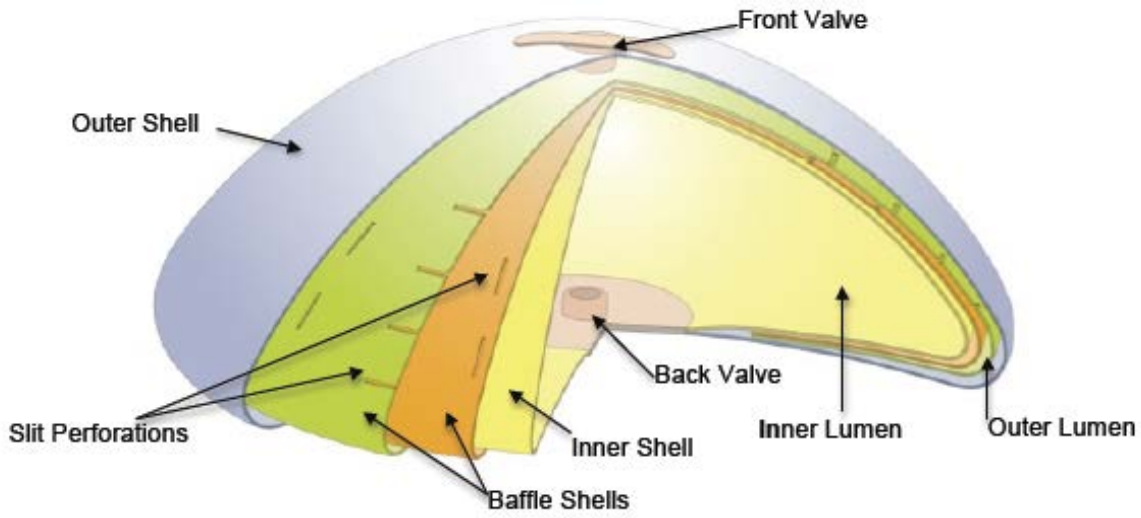


**Figure 1:** Cut-away drawing of IDEAL IMPLANT (335 cc to 555 cc size) to show internal structure

**Table 1:** Implant Volumes and Amount of Baffle Material (Shells)

| Implant Size | Empty Implant Volume | Inner Lumen Fill Volume | Baffle Shells | Outer Lumen Fill at "High" | Outer Lumen Fill at "100%" | Total Implant Volume Range |
|---|---|---|---|---|---|---|
| 210 cc | 30 cc | 120 cc | 1 | 60 cc | 85 cc | 210-235cc |
| 240 cc | 33 cc | 142 cc | 1 | 65 cc | 95 cc | 240-270cc |
| 270 cc | 35 cc | 165 cc | 1 | 70 cc | 105 cc | 270-305cc |
| 300 cc | 37 cc | 188 cc | 1 | 75 cc | 115 cc | 300-340cc |
| 335 cc | 52 cc | 188 cc | 2 | 95 cc | 135 cc | 335-375cc |
| 370 cc | 56 cc | 214 cc | 2 | 100 cc | 145 cc | 370-415cc |
| 405 cc | 60 cc | 235 cc | 2 | 110 cc | 160 cc | 405-455cc |
| 440 cc | 64 cc | 261 cc | 2 | 115 cc | 170 cc | 440-495cc |
| 475 cc | 68 cc | 287 cc | 2 | 120 cc | 180 cc | 475-535cc |
| 515 cc | 72 cc | 318 cc | 2 | 125 cc | 190 cc | 515-580cc |
| 555 cc | 76 cc | 344 cc | 2 | 135 cc | 205 cc | 555-625cc |
| 595 cc | 94 cc | 346 cc | 3 | 155 cc | 230 cc | 595-670cc |
| 635 cc | 102 cc | 373 cc | 3 | 160 cc | 235 cc | 635-710cc |
| 675 cc | 110 cc | 405 cc | 3 | 160 cc | 240 cc | 675-755cc |

The IDEAL IMPLANT comes in one style as described in Table 2. Table 3 shows the implant materials.

**Table 2:** Approved IDEAL IMPLANT Saline-filled Breast Implants

| | Shape | Implant Size (cc) | Diameter (cm) | Projection (cm) | Shell Thickness (in) | Baffle Shells |
|---|---|---|---|---|---|---|
| Smooth | Round | 210-675 | 9.8-14.2 | 4.0-5.8 | 0.014-0.028 | 1-3 |

**Table 3:** Implant Materials

| Component | NuSil Material | Method of Cure/ Vulcanization Used |
|---|---|---|
| Shells (inner, outer and baffles) | MED-6605 RTV Cure Silicone Dispersion | Acetoxy / RTV |
| Valve | MED-4860 Liquid Silicone Rubber | Platinum / HTV |
| Valve Strap | MED-4850 Liquid Silicone Rubber | Platinum / HTV |
| Patch (vulcanized) | MED-4750 Silicone Elastomer | Platinum / HTV |
| Patch (un-vulcanized) | MED-2174 Silicone Elastomer | Peroxide / NA |

## VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several other alternatives to augmentation of the breast with saline-filled breast implants, including silicone gel-filled implants, fat injections, mastopexy with an implant, external prostheses or no treatment. Each alternative has its own advantages and disadvantages. A patient should fully discuss these alternatives with her physician to select the method that best meets expectations and lifestyle.

## VII. MARKETING HISTORY

The IDEAL IMPLANT has not been marketed in the United States or any foreign country.

## VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Below is a list of the potential adverse effects (e.g., complications) associated with the use of the device.

- Deflation
- Capsular contracture
- Reoperation
- Implant removal (with or without replacement)
- Pain
- Changes in nipple and breast sensation
- Infection
- Scarring
- Asymmetry
- Wrinkling

- Implant displacement/migration
- Implant palpability/visibility
- Breastfeeding complications
- Hematoma/seroma
- Implant extrusion
- Necrosis
- Delayed wound healing
- Breast tissue atrophy/chest wall deformity
- Calcium deposits
- Lymphadenopathy
- Ptosis
- Difficulty in mammogram interpretation
- Toxic shock syndrome
- Connective tissue disease (CTD)
- CTD signs and symptoms
- Lymphoma
- Cancer
- Anesthesia complications
- Neurologic complications
- Reproductive problems
- Suicide
- Dissatisfaction with cosmetic results
- Skin scar unsatisfactory
- Mastopexy unsatisfactory
- Implant position unsatisfactory (malposition)
- Mastitis
- Dissatisfaction with implant size selected
- Breast lesion

For the specific adverse events that occurred in the clinical study, please see Section X below.

## IX. SUMMARY OF PRECLINICAL STUDIES

The preclinical studies are divided into five sections: chemistry, toxicology, mechanical, modes and causes of failure, and shelf life.

### A. Chemistry Data

#### 1. Extent of Cross-linking

The extent of cross-linking was measured on implant shells produced from three lots of raw material. The percent weight gain and crosslink density were both uniform over the three lots tested. Mechanical testing of the cured shells demonstrated that the

extent of cross-linking of the silicone used in the shell is sufficient to ensure that the shells meet the requirements of ASTM F2051 and ISO 14607.

The extent of crosslinking was also determined by solvent extraction on devices produced from four production lots. The percent crosslinking was uniform for the four lots tested and ranged from 96.9% to 97.4%, or a degree of crosslinking equal to 4.8 – 5.3 crosslinks per molecule. Young's Modulus at low strain is approximately proportional to cross-link density and was also consistent across several implant lots.

Gel Permeation Chromatography (GPC) testing was performed on solvent extractions of shell material to evaluate the molecular weight and distribution of molecular weights for the materials extracted. The Polydispersity Index (PDI), the ratio of weight average molecular weight to number average molecular weight, was measured and found to be 2.1 – 2.2.

Infrared (IR) spectroscopy is the study of molecular vibrations that provides specific information about chemical bonding and molecular structure of organic substances. FTIR-Attenuated Total Reflectance (ATR) analyses of shell and patch material were consistent with polydimethylsiloxanes. FTIR analysis on solvent-extracted residue resulted in an infrared spectrum with similar major bands as the ATR analysis at the wavelengths 2965, 1098, 1020, and 864 $cm^{-1}$. These major wavelength bands were nearly identical to a reference scan of polydimethylsiloxane.

**2. Extractables**

Exhaustive solvent extractions were carried out on test articles cut from finished, dry-heat sterilized IDEAL IMPLANTS comprised of silicone shell, patch, valve and valve strap components, followed by gas chromatography-mass spectrometry (GC-MS) and gas chromatography-flame ionization detector (GC-FID) analyses. The solvents used included water, ethanol, methylene chloride, and hexane. Hexane solvent was selected for subsequent siloxane quantitation because it extracted the highest weight percent solids relative to water, ethanol, and methylene chloride. Table 4 summarizes the test results for hexane-extracted linear and cyclic siloxanes having a size of 1500 Daltons or less over four lots of finished, sterilized implants. The practical quantitative limit for the cyclic and linear siloxanes was 0.1 µg/g.

In addition to cyclic and linear siloxanes, the compounds 1,2-diphenyltetramethyldisilane, ethanedioic acid, bis(trimethylsilyl)ester, 1,3,5-tris(trimethylsiloxy)benzene, octadecanoic acid, butyl ester, hexadecanoic acid, butyl ester, cyclohexane, and tetrahydro-2,5- dimethylfuran were detected and quantitated by GC-MS analysis of extracts. There were no solvent residuals detected in the GC-MS analysis of extractions with a practical quantitative limit of 13 µg/g. The concentrations of these species were evaluated by a toxicological risk assessment and found to present no toxicological concerns.

Exhaustive extractions of finished, dry heat sterilized implants were also analyzed for polychlorinated biphenyls (PCBs). The TEQ (WHO-2005 Mammal) was found to be <0.0001 picograms/g implant, which poses no toxicological concerns.

**Table 4:** Hexane Extracted Siloxanes (<1500 Daltons or amu) in Finished Sterilized Implants

| Siloxane | Molecular Weight (amu) | Quantity in Implant (µg/g) |
|---|---|---|
| Cyclic Siloxanes | | |
| $D_4$ | 296 | 0.0 – 4.3 |
| $D_5$ | 370 | 0.2 – 15.0 |
| $D_6$ | 444 | 0.7 – 48.0 |
| $D_7 – D_{21}$ | 518 – 1554 | 4,083 – 11,188 |
| All Cyclic $D_4 – D_{21}$ | 296 – 1554 | 4,084 – 11,256 |
| Linear Siloxanes | | |
| $MD_2M$ | 310 | 0.0 – 1.1 |
| $MD_3M$ | 384 | 0.0 – 2.2 |
| $MD_4M$ | 458 | 0.0 – 2.1 |
| $MD_5M – MD_{19}M$ | 532 – 1568 | 5.0 – 193 |
| All Linear $MD_2M – MD_{19}M$ | 310 – 1568 | 5.0 – 199 |
| | | |
| Total Extractables | | 2.6 – 3.1% by weight |

The extractable testing results are comparable to results seen in previously approved saline-filled breast implant devices.

### 3. Volatiles

Sterilized silicone shell material was analyzed for volatiles using GC-MS headspace methodologies. Isopropanol, a processing aid, was detected at 0.9 micrograms per gram (0.9 ppm), but does not pose any toxicological risk by toxicological risk assessment. All other compounds were below detectable limits (including xylene) of 0.05 to 1.0 µg/g, depending on the specie. The volatiles testing results are comparable to results seen in previously approved breast implant devices

### 4. Heavy Metals

Inductively Coupled Plasma (ICP) Spectroscopy was performed on implants and implant components to determine the trace elements/metals content. Implants and shells were also analyzed by ICP after being completely ashed and acid-digested. The metals found in the implant are shown in Table 5, expressed as ppm in the implant. The concentrations of the elements in Table 5 do not pose any toxicological concerns based on a comprehensive toxicological risk assessment.

The same platinum catalyst is used in the manufacture of certain components in all gel-filled and saline-filled breast implants, including: valve, patch, valve strap, HTV shell and silicone gel filler. While a large amount of platinum catalyst is used for the HTV shell and silicone gel filler in silicone gel-filled implants, the IDEAL IMPLANT uses only a small amount of platinum catalyst for the patch, valve, and valve strap. A minute amount of platinum catalyst may remain in breast implant components and may enter the body by diffusion. However, FDA has concluded that the platinum contained in breast implants is in the zero oxidation state, which has the lowest toxicity, and thus, does not pose a significant risk to women with breast implants. The "FDA Backgrounder on Platinum in Silicone Breast Implants" at the FDA website http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/ImplantsandProsthetics/BreastImplants/UCM064040, states that:

"Based on the existing literature, FDA believes that the platinum contained in breast implants is in the zero oxidation state, which would pose the lowest risk, and thus that the small amounts of platinum that leak through the shell do not represent a significant risk to women with silicone breast implants."

**Table 5:** Maximum Metals Content Based on Whole Implant or Shells

| Element | Concentration (µg/g or ppm) |
|---|---|
| Arsenic, Beryllium, Cadmium, Cobalt, Molybdenum, Selenium, Silver, Thallium, Titanium, and Vanadium | BDL* |
| Aluminum | BDL – 6.3 |
| Antimony | BDL – 0.38 |
| Barium | BDL – 0.25 |
| Calcium | BDL – 90 [a] |
| Chromium | BDL – 5.0 |
| Copper | BDL – 0.35 |
| Iron | 1.1 – 23 |
| Lead | BDL – 1.5 |
| Magnesium | BDL – 12 |
| Manganese | BDL – 0.95 |
| Nickel | BDL – 2.9 |
| Phosphorous | 3.5 – 5.8 |
| Platinum | BDL – 2.5 [b] |
| Potassium | BDL – 20 |
| Sodium | BDL – 3.4 |
| Tin | BDL – 10.5 |
| Zinc | BDL – 80 [c] |

* BDL is Below Detectable Limits
a – 90 µg/g in patch, and patch is approximately 10% of the whole implant weight
b – 2.5µg/g in patch, and patch is approximately 10% of the whole implant weight
c – 80 µg/g in patch, and patch is approximately 10% of the whole implant weight

The heavy metal analysis results are comparable to results seen in previously approved saline-filled breast implant devices.

## B. Toxicology Data

Ideal Implant performed a toxicological risk assessment and Margin of Safety (MOS) analysis per ISO 10993-17 to address the pharmacokinetics of implant extractables, and biocompatibility testing, including carcinogenicity and reproductive and developmental toxicity, to address the biological safety of the material.

### 1. Pharmacokinetics

The pharmacokinetic behavior of potentially toxic chemicals is an assessment of the potential for the chemicals to accumulate in the body, with or without metabolism or excretion, at concentrations that may cause human health risks.

The pharmacokinetics of the IDEAL IMPLANT has been addressed through a toxicological risk assessment based on exhaustive solvent extractions and whole implant ashing/acid digestion followed by quantitative analysis. The MOS approach was used to assess the safety of the extracted compounds including metals, siloxanes and organic compounds. All calculated MOS values for metals, siloxanes, and organic compounds were much greater than 1.

The lower molecular weight cyclic siloxanes, D4-D6, were found to have MOS values of 28,000 or higher, demonstrating that any release of D4-D6 from the implants should not pose any toxicological concerns or adverse systemic effects in patients.

The results are comparable to results seen in previously approved breast implant devices.

### 2. Biocompatibility Testing

Biocompatibility testing was conducted on finished, dry heat sterilized implants and/or implant components per the appropriate ISO, ASTM and/or EPA methods and guidelines. The results are summarized in Table 6.

**Table 6:** Summary of Biocompatibility Testing

| Test | Purpose | Acceptance Criteria | Results |
|---|---|---|---|
| Irritation | Test article: Extracts of finished, sterilized implant<br><br>Purpose is to evaluate the potential for a test article to cause irritation following intracutaneous injection of extracts in rabbits (based on ISO 10993-10). The test article is extracted in 0.9% sodium chloride USP solution and sesame oil and injected in the animal at 5 sites. | The difference between each test extract overall mean score and corresponding control overall score is 1.0 or less. | No erythema or edema from NaCl extract; slight erythema and very slight edema from sesame oil extract. Difference between mean control score was 1.0 or less. |
| Sensitization | Test article: Extracts of finished, sterilized implant.<br><br>Purpose is to evaluate the potential to cause delayed dermal contact sensitization in a guinea pig maximization test (based on ISO 10993-10). The test article is extracted in 0.9% sodium chloride USP solution and sesame oil and then intradermally injected and occlusively patched to the animal. | No delayed dermal contact sensitization. Grades of 1 or greater observed in the test group generally indicate sensitization, provided grades of less than 1 were observed on the control animals. | No evidence of causing delayed dermal contact sensitization from NaCl or sesame oil extracts. Dermal reaction scores were less than 1. |
| Cytotoxicity | Test article: Extracts of finished, sterilized implant<br><br>Purpose is to evaluate potential cytotoxicity effects following ISO 10993-5. The test article is extracted in single strength Minimal Essential Medium (1X MEM). Triplicate monolayers of L-929 mouse fibroblast cells are then dosed with the extract and incubated. | No evidence of causing cell lysis or toxicity, and a Grade 2 or less. | 1X MEM test extract showed no evidence of causing cell lysis or toxicity. Grade was less than<br>2 (mild reactivity). |

| Test | Purpose | Acceptance Criteria | Results |
|---|---|---|---|
| Acute Systemic Toxicity | Test articles: Extracts of finished, sterilized implant, implant shells, and finished, sterilized FTA.<br><br>This testing includes extract systemic toxicity, pyrogenicity, and LAL. The purpose of these tests is to evaluate the systemic toxicity of test article extracts following ISO 10993 guidelines. | No evidence of systemic toxicity, non-pyrogenic, and <20 EU/device | There was no mortality or evidence of systemic toxicity from NaCl or sesame oil extracts. The test article was judged as non-pyrogenic. Bacterial endotoxin test results were all less than the FDA and USP guidelines of 20 EU/device. |
| Hemocompatibility | Test article: Finished, sterilized implant<br><br>Purpose is to evaluate potential to cause hemolysis based on ASTM F756 and ISO 10993-4. Anticoagulated whole rabbit blood is pooled, diluted and added to tubes containing the test article. | Test article is non-hemolytic (hemolytic index of <2%) | The mean hemolytic index for both extract and test article in CMF-PBS was 0%; both were non-hemolytic. |
| Immunotoxicity | Test article: Finished, sterilized implant<br><br>Purpose is to evaluate the potential immunological effects of the test article via subcutaneous exposure to B6C3F1 female mice for a minimum of 28 days. The assessment is based on NK cell assay, AFC assay, immunophenotyping of splenic cell subpopulations, and anti-CD-3 T-cell proliferation. In addition, thymus and spleen organ weights and hematology parameters are evaluated. | No adverse effects on humoral, innate, or cell-mediated components of the immune system. | Subcutaneous implantation in female B6C3F1 mice resulted in no adverse effects on the humoral, innate, or cell-mediated components of the immune system. |

| Test | Purpose | Acceptance Criteria | Results |
|---|---|---|---|
| Reproductive and Developmental Toxicity | Test article: Finished, sterilized implant<br><br>Purpose is to evaluate the potential adverse effects of the implanted test article on the reproductive capabilities, including gonadal function, estrous cyclicity, mating behavior, conception, gestation, parturition, lactation, and weaning of $F_0$ and $F_1$ generations and $F_1$ and $F_2$ neonatal survival, growth, and development. Conducted in accordance with ISO 10993-3 and OECD guidelines 414 and 416. | No systemic, reproductive, developmental, or neonatal toxicity. | Two-generation subcutaneous implantation of the IDEAL IMPLANT in female Crl:CD(SD) rats resulted in no systemic, reproductive, developmental, or neonatal toxicity. |
| Genotoxicity | Test article: Extracts of finished, sterilized implant, and extracts of shell, valve and patch.<br><br>The Bacterial Reverse Mutation Study evaluates if test article extracts will induce reverse mutations at the histidine locus of the *Salmonella typhimurium* tester strains TA98, TA100, TA1535, and TA1537 or at the tryptophan locus of *Escherichia coli* tester strain WP2uvrA. The Mouse Lymphoma Assay evaluates the genotoxic potential of a test article by detecting both gene mutation and chromosomal damage. The Mouse Peripheral Blood Micronucleus Study evaluates genotoxicity potential from the % micronucleated reticulocytes (MN-RET). | Not mutagenic, not genotoxic, no cellular toxicity, and no micronuclei induced in mice. | The test article extract was considered to be non-mutagenic. The test articles were not considered to be genotoxic; No evidence of cellular toxicity or induced micronuclei. |

| Test | Purpose | Acceptance Criteria | Results |
|---|---|---|---|
| Carcinogenicity | Test article: Finished, sterilized implant<br><br>Purpose is to evaluate the potential for an implanted test article to induce tumor formation (cancer) over a test period of 26 weeks in the transgenic rasH2 mouse model. | No increase in tumor formation (tumorogenicity) relative to a negative control test article. | The test article did not demonstrate an increased incidence of tumor formation (tumorogenicity) relative to the negative control following subcutaneous implantation in a transgenic mouse model. |
| Implantation | Test articles: Finished, sterilized implant, and shell, patch and valve strap.<br><br>The purpose of muscle implantation studies was to evaluate evidence of irritation or toxicity after implantation of the test article in muscle tissue of the rabbit, based on ISO 10993-6. The purpose of subcutaneous implantation studies was to evaluate the potential for subchronic systemic toxicity in the rat, based on ISO 10993-11 | A macroscopic Reaction Index difference of 0.0 to 0.5 is considered "not significant", and a macroscopic score of 0.0-2.9 is considered to be a non-irritant. | The macroscopic reaction was insignificant (score <0.5) and the test article was classified as non-irritant (score <2.9) after 2 and 12 weeks of rabbit muscle implantation, and 4 and 26 weeks of rat subcutaneous implantation. No significant evidence of systemic toxicity. |

The toxicology testing results are comparable to results seen in previously approved saline-filled breast implant devices.

## C. Mechanical Data

1. Percent Elongation (Ultimate Elongation) Test

Percent Elongation at failure, or Ultimate Elongation, is a tensile test based on strain. Implant shells from finished, sterilized implants (sizes 210cc, 300cc, 335cc, 370cc, 405cc, 440cc, 475cc, 635cc and 675cc) were tested according to test method ASTM F2051 for percent elongation. The results were evaluated against the acceptance criteria according to ASTM F2051 and ISO 14607. All implant shells passed the ASTM F2051 requirement (≥350%) and ISO 14607 requirement (≥450%).

2. Load at Break Test

Load at Break, or breaking strength, is a tensile test based on force. Implant shells from finished, sterilized implants (sizes 210cc, 300cc, 335cc, 370cc, 405cc, 440cc, 475cc, 635cc and 675cc) were tested according to ASTM F2051 for load at break. The results were evaluated against the acceptance criteria according to ASTM F2051. All implant shells passed the ASTM F2051 requirement (≥2.5 $lb_f$).

3. Tensile Set Test

Tensile Set is a tensile test that evaluates the residual elongation of a test sample after being stretched and allowed to relax in the specified manner. Implant shells from finished, sterilized implants (sizes 210cc, 300cc, 335cc, 370cc, 405cc, 440cc, 475cc, and 635cc, 675cc) were tested according to test methods ASTM F2051 and ISO 14607. All implant shells passed the ASTM F2051 and ISO 14607 requirement (<10% after 3 minutes at 300% elongation).

4. Joint Integrity Test

Joint integrity testing is performed to determine the strength of critical and non-critical vulcanized joints. Critical joints include the shell-patch, valve-shell, and valve-patch. The shell-patch and valve-shell joints are tested according to ASTM F2051 and ISO 14607. These critical joints passed the ASTM F2051 requirement (no failure after 200% elongation for 10 seconds) and ISO 14607 requirement (no failure after 300% elongation for 10 seconds). Due to the unique design of the IDEAL IMPLANT, the critical valve-patch joint cannot be tested using ASTM or ISO standards. Instead, this joint is tested using a custom method requiring a strength of 20 lbf or greater before failure. All valve-patch joints from finished sterilized implants passed this requirement. The valve strap-shell joints are considered non-critical. These non-critical joints passed the ASTM F2051 and ISO 14607 requirement (no failure after 100% elongation for 10 seconds).

5. Valve Competence Test

Valve competence testing evaluates the seal of the anterior and posterior valves on the IDEAL IMPLANT. The valves are subjected to retrograde pressure of saline and observed for leaks. The anterior ("front") and posterior ("back") valves are identical in the IDEAL IMPLANT, and were tested according to ASTM F2051 and ISO 14607. All front and back valves passed the requirements of these standards (no leaks after 5 minutes at retrograde pressures of 3 cm and 30 cm of water).

6. Fatigue Testing

Static Burst Testing

Static burst testing was conducted on implants to determine the maximum compressive force that an implant can withstand before failure. Worst-case, finished, dry heat sterilized implants (three (3) size 210cc and three (3) size 595cc) were subjected to static burst testing until failure. The implants withstood 3,420 – 5,155 lbs of force before failure.

Cyclic Fatigue Testing

Cyclic fatigue testing was conducted on implants to determine the number of cycles for various loads at which implants fail, and to determine the endurance load at which the implant does not fail. Worst-case, finished, dry-heat sterilized implants (Eighteen (18) size 210cc and three (3) size 595cc) were tested. The testing was conducted in air at ambient temperature over the frequency range of 0.8 to 2 Hz at various loads to either run out (6.5 million cycles without rupture) or failure. The endurance load for the smallest worst-case implant was 22 lbf. The endurance load acceptance criteria of 1.8 lbf or greater was met for this worst-case implant. The endurance load for the largest worst-case implant was 25 lbf. The endurance load acceptance criteria of 5.4 lbf or greater was met for this worst-case implant. The measured endurance loads are also 2-42 times greater than estimated cyclic in vivo loads.

A total of six (6) worst-case, finished, dry-heat sterilized implants (size 210cc) were also subjected to 2 million fatigue cycles and impact resistance testing per ISO 14607. The IDEAL IMPLANT met all requirements per this standard.

The results of the mechanical testing are comparable to results seen in approved breast implants.

**D. Modes and Causes of Failure**

Implant failures were indicated by deflation. Explants due to deflation were evaluated for cause of the implant failure. A total of 1004 implants manufactured at the original IDE manufacturing site were implanted at the start of the clinical trial, of which 31 failed. Of the 1004 implants, 87 had the initial design (6.3mm diameter) valve attachment component and 8 deflated due to an inadequate vulcanization bond. (This design defect was updated in a manufacturing change). Of the 1004 implants, 917 had the final design (8mm diameter) valve attachment component and 23 deflated due to early pilot-scale manufacturing defects related to joint vulcanization and assembly processes. (These early manufacturing defects were addressed at the PMA commercial-scale manufacturing site with improved process controls and inspections.)

A total of 49 additional implants manufactured at the original IDE manufacturing site were implanted as replacement implants during the course of the 2-year follow-up period, for reasons such as deflation or size change. All 49 had the final design (8mm diameter) valve attachment component and 0 deflated.

### E. Shelf Life

Shelf life testing was performed on implants and the implant dual tray package. Implant mechanical testing, before and after aging, was performed according to ASTM standard F2051 and ISO 14607. All mechanical properties, including ultimate load at break, ultimate elongation, tensile set, adhered joint strength, and valve competency, met the requirements in ASTM F2051 and ISO 14607. Package testing was performed according to ASTM standards F1929 and F88 for dye penetration and seal strength, respectively. All dual tray packages met the acceptance criteria of the testing protocols.

Accelerated and real-time aging test results were used to establish the shelf life of the IDEAL IMPLANT. The resulting data supports a 3-year shelf life for the IDEAL IMPLANT.

## X. SUMMARY OF PRIMARY CLINICAL STUDY

Ideal Implant Incorporated performed a clinical study to establish a reasonable assurance of safety and effectiveness of IDEAL IMPLANTS for breast augmentation and breast augmentation revision in the US under IDE # G080055. Data from this clinical study were the basis for the PMA approval decision. A summary of the clinical study is presented below.

Early in the trial, the diameter of the valve attachment component was increased from 6.3mm to 8mm to improve bond strength, which reduced the risk of spontaneous deflation, subsequent operations and implant removal, as shown in Table 7. Late in the trial, the baffle perforations were holes instead of slits. Approval is not requested for either the 6.3mm diameter valve attachment component implant, or the baffle hole perforations implant. The results of the clinical study include pooled analysis of the 8mm and 6.3mm diameter valve attachment component implants. There were 456 subjects (912 implants) who initially received the final version (8mm valve attachment component) of the device bilaterally, and 5 subjects (5 implants) who initially received the final version of the device unilaterally. The distribution of these implants in the clinical trial is shown in Table 1.

**Table 7:** Kaplan-Meier Failure Rates for Adverse Events at 2 years for Initial Bilateral 6.3mm and 8mm Valve Attachment Component Implants, per Subject

| | **Primary Augmentation** | | **Revision Augmentation** | |
|---|---|---|---|---|
| **Event** | **6.3mm N=31*** | **8mm N=363*** | **6.3mm N=10** | **8mm N=93** |
| All subsequent breast operations | 32.3% (18.8%, 51.6%) | 14.2% (11.0%, 18.3%) | 50.0% (24.7%, 81.6%) | 23.7% (16.3%, 33.7%) |
| Implant removal with or without replacement | 22.6% (11.5%, 41.6%) | 7.5% (5.2%, 10.8%) | 10.0% (1.5%, 52.7%) | 15.1% (9.2%, 24.2%) |

| | | | | |
|---|---|---|---|---|
| Spontaneous deflation | 19.4% (9.2%, 38.1%) | 4.8% (3.0%, 7.6%) | 10.0% (1.5%, 52.7%) | 3.3% (1.1%, 10.0%) |

* 5 subjects who received a 6.3mm valve attachment implant on one side and an 8mm valve attachment implant on the other side are not included

## A. Study Design

Patients were treated between February 5, 2009 and February 4, 2010. The database for this PMA reflected data collected through April 30, 2012 and included 502 patients. There were 35 investigational sites.

The study is a 10-year prospective, multi-center, open label study of the IDEAL IMPLANT in which subjects served as their own controls for the evaluation of effectiveness. Two patient cohorts were enrolled in the study:

- Adult women undergoing bilateral primary augmentation ("Primary Augmentation Cohort"); and
- Adult women undergoing bilateral revision of existing saline-filled or silicone gel-filled augmentation implants ("Revision Augmentation Cohort").

The clinical trial protocol specifies a 10-year study with data analysis and submission of a premarket approval (PMA) application after the last subject completed the 2-year follow-up visit. This application provides the safety and effectiveness data collected and analyzed through these 2-years of follow-up visits.

1. Clinical Inclusion and Exclusion Criteria

   Enrollment in the clinical study was limited to patients who met the following inclusion criteria

   - Is a genetic female, 18 years of age or older
   - Is a US citizen and primarily resides within 100 miles of investigator
   - Has an e-mail address
   - Bilateral primary breast augmentation - has dissatisfaction with breast size and wishes breast enlargement,
     OR
     Bilateral revision augmentation - has had previous augmentation with silicone gel-filled or saline-filled implants
   - Agrees to sign the Informed Consent form, including HIPAA authorization
   - Agrees to sign a Medical Records Release form
   - Agrees to comply with post-operative instructions
   - Agrees to follow the procedures for explant analysis including to authorize return of the implant to Ideal Implant Incorporated if the implant is explanted
   - Agrees to comply with follow-up requirements including e-mail contacts, visits, and questionnaires

Patients were not permitted to enroll in the clinical study if they met any of the following exclusion criteria:

- Plans to become pregnant within six months of the procedure
- Has nursed a child within three months of study enrollment
- Has a condition that could compromise or complicate wound healing
- Has a diagnosis of active cancer of any type
- Has ever been diagnosed with breast cancer
- Has pre-malignant breast disease
- Has an infection or abscess anywhere in the body
- Has tissue characteristics incompatible with an implant, such as inadequate tissue cover or compromised vascularity
- Has any condition, or is under treatment for any condition which, in the opinion of the investigator, may constitute an unwarranted surgical risk
- Has an anatomic or physiologic abnormality that could lead to significant post-operative adverse events
- Has unrealistic/unreasonable expectations of the procedure results

2. Follow-up Schedule

Within 30 days of the baseline visit, qualified subjects were to be implanted with IDEAL IMPLANTS. All patients were scheduled to return for follow-up examinations at 2 months, 6 months, 1, 2, 3, 4, 5, 6, 7, 8, 9 and 10 years post-implant. At each follow-up visit, the protocol specifies that subjects are to be examined, the implants assessed, the extent of capsule graded according to the Baker classification scheme, and patient/investigator satisfaction assessed. At 6 months and 1 year, chest measurements are to be made. At 1, 2, 4, 6, 8 and 10 years, the protocol specifies that subjects are to complete the Breast Evaluation Questionnaire and the SF-36 Questionnaire. At 1, 2, 4, 7, and 10 years, the protocol specifies that subjects are to complete the Rheumatologic and Connective Tissue Disease Screen (CTDS). Adverse events are to be documented throughout the 10-year study.

The key time points are shown in Tables 8 below, summarizing safety and effectiveness.

**Table 8:** Study Follow-Up Schedule

| **Data Collected** | **Timeframe** | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | **Baseline** | **2 mo** | **6 mo** | **1 year** | **2 year** | **3 year** | **4 year** | **5 year** | **6 year** | **7 year** | **8 year** | **9 year** | **10 year** |
| Enrollment Screen | X | | | | | | | | | | | | |
| Breast History | X | X | X | X | X | X | X | X | X | X | X | X | X |
| Medical History | X | X | X | X | X | X | X | X | X | X | X | X | X |
| Subject Examined | X | X | X | X | X | X | X | X | X | X | X | X | X |

| Data Collected | Timeframe | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | **Baseline** | **2 mo** | **6 mo** | **1 year** | **2 year** | **3 year** | **4 year** | **5 year** | **6 year** | **7 year** | **8 year** | **9 year** | **10 year** |
| Implants Assessed | | X | X | X | X | X | X | X | X | X | X | X | X |
| Baker Classification Graded | | X | X | X | X | X | X | X | X | X | X | X | X |
| Patient/Investigator Satisfaction Assessed | | X | X | X | X | X | X | X | X | X | X | X | X |
| Chest Measurements * | X | | X | X | | | | | | | | | |
| Breast Evaluation Questionnaire and SF-36 Questionnaire | X | | | X | X | | X | | X | | X | | X |
| Rheumatic and CTD Screens | X | | | X | X | | X | | | X | | | X |
| Adverse Events | | X | X | X | X | X | X | X | X | X | X | X | X |

*Primary Augmentation Cohort only

3. Clinical Endpoints

With regards to safety, the safety study endpoint was that use of the IDEAL IMPLANT elicits an acceptable safety profile. In general, the safety of the IDEAL IMPLANT was assessed through the incidence and timing of all adverse events collected throughout the study.

With regards to effectiveness, five effectiveness endpoints were evaluated:

- Increase in breast size for Primary Augmentation Cohort only
- Breast Evaluation Questionnaire (BEQ)
- Patient satisfaction with outcome
- Investigator satisfaction with outcome
- SF-36 Questionnaire

4. Statistical Analyses

The clinical study data collected through 2 years of follow-up were analyzed. The risk of occurrence of adverse events (for example, subsequent breast operations and device removals with or without replacement) were estimated using Kaplan-Meier rates of first occurrence; data were analyzed for each cohort separately (Primary Augmentation and Revision Augmentation). Subsequent breast operations and device removals with or without replacement (explants) were analyzed to provide a frequency distribution of the reasons for the procedures. Effectiveness analyses included a comparison of the increase in breast size from baseline to 1 year for the Primary Augmentation Cohort only. Responses to the BEQ and SF-36 were analyzed for changes between baseline and post – implantation results at 1 and 2 years. Patient satisfaction and investigator satisfaction were analyzed as well at 1 and 2 years.

The results through 2 years are reported, while the study remains ongoing. Data will continue to be analyzed and reported to FDA at regular study intervals. In addition, the Sponsor will periodically update labeling as more data and information become available.

## B. Accountability of PMA Cohort

At the time of database lock, of 502 patients enrolled in the PMA study, 94% (472) patients are available for analysis at the 2-year post-operative visit. Five hundred and two subjects (502) underwent device implantation (399 in the Primary Augmentation Cohort and 103 in the Revision Augmentation Cohort) and were enrolled at 35 investigational sites. All investigators and investigational sites were private practice plastic surgeons certified by the American Board of Plastic Surgery, providing the opportunity to assess the performance of the device at medical practices consistent with commercial use. Table 9 shows the subject disposition and follow-up rates over the course of 2 years. Subject follow-up rates were ≥ 97% at all follow-up visits. The high and consistent follow-up rates provide a statistically robust and unbiased sample size upon which to evaluate device safety and effectiveness.

**Table 9:** Subject Disposition and Cumulative Subject Follow-up for the Primary Augmentation Cohort and the Revision Augmentation Cohort

| Cohort | Subject Status | Follow up Time Interval | | | |
|---|---|---|---|---|---|
| | | 2 Months | 6 Months | 1 Year | 2 Year |
| Primary Augmentation | Theoretically due [A] | 399 | 399 | 399 | 399 |
| | Deaths | 0 | 0 | 0 | 0 |
| | All devices removed and replaced with other manufacturer's devices | 0 | 3 | 7 | 7 |
| | Voluntary withdrawal by subject | 0 | 1 | 3 | 6 |
| | Expected [B] | 399 | 395 | 389 | 386 |
| | Actual (Complete follow-up) | 397 | 391 | 383 | 378 |
| | Lost to follow-up | 2 | 4 | 6 | 8 |
| | Percent follow-up (Actual/Expected) | 99.4% | 98.9% | 98.4% | 97.9% |
| Revision Augmentation | Theoretically due [A] | 103 | 103 | 103 | 103 |
| | Deaths | 0 | 0 | 0 | 0 |
| | All devices removed and replaced with other manufacturer's devices | 0 | 2 | 5 | 7 |
| | Voluntary withdrawal by subject | 0 | 0 | 0 | 0 |
| | Expected [B] | 103 | 101 | 98 | 96 |
| | Actual (Complete follow-up) | 103 | 101 | 96 | 94 |
| | Lost to follow-up | 0 | 0 | 2 | 2 |
| | Percent follow-up (Actual/Expected) | 100% | 100% | 97.9% | 97.9% |

[A] Subjects who would have been examined according to date of implantation and follow-up schedules.

[B] Subjects who are theoretically due minus the sum of the deaths, voluntary withdrawals and removals with replacement with different manufacturer's implants.
Subjects with voluntary withdrawal or lost to follow-up date after a visit window in which they did not actually attend were counted as withdrawn in the relevant category at that missed visit.

## C. Study Population Demographics and Baseline Parameters

Table 10 shows the subject demographics and medical history for the women in the Primary Augmentation Cohort and the Revision Augmentation Cohort

**Table 10:** Subject Demographics and Medical History per Subject

| Measure | Primary Augmentation (N=399) | Revision Augmentation (N=103) |
|---|---|---|
| Age (years) [1] | 34.5±10.4 (399)<br>34.0 [18.0, 68.0] | 46.7±9.3 (103)<br>47.0 [21.0, 67.0] |
| Race [2] | | |
| American Indian Alaska Native | 1.3% (5/399) | 0% (0/103) |
| Asian | 3.0% (12/399) | 1.9% (2/103) |
| Black/African American | 5.0% (20/399) | 1.9% (2/103) |
| Native Hawaiian / Pacific Islander | 0.8% (3/399) | 0% (0/103) |
| Caucasian | 82.7% (330/399) | 83.5% (86/103) |
| Other | 9.5% (38/399) | 14.6% (15/103) |
| Ethnicity | | |
| Hispanic or Latino | 11.8% (47/399) | 14.6% (15/103) |
| Non-Hispanic or Latino | 88.2% (352/399) | 85.4% (88/103) |
| BMI ($kg/m^2$) | 22.3±3.6 (399)<br>21.6 [14.4, 53.2] | 22.4±3.9 (103)<br>21.5 [18.1, 48.7] |
| Any Pregnancy History | 73.9% (295/399) | 89.3% (92/103) |
| Number of pregnancies | 2.6±1.4 (295)<br>2.0 [1.0, 8.0] | 2.6±1.4 (92)<br>2.0 [1.0, 7.0] |
| Number of live births | 2.1±1.2 (295)<br>2.0 [0.0, 7.0] | 2.0±1.0 (92)<br>2.0 [0.0, 5.0] |
| Baseline Chest Circumference | | |
| Inframammary fold | 31.0±2.9 (397)<br>30.5 [24.0, 42.0] | 30.8±3.1 (102)<br>30.0 [26.5, 45.0] |
| Nipples | 34.6±3.1 (397)<br>34.0 [27.5, 45.5] | 36.7±3.2 (102)<br>36.5 [30.5, 48.5] |

Numbers are Mean ± SD (N), Median [Min, Max] for continuous measures and Percent (Count/N) for discrete measures.
[1] Age calculated at date of implant.
[2] More than one race category may be selected for each subject

Table 11 shows the operative details per implant for women in the Primary Augmentation and the Revision Augmentation Cohorts. The inframammary incision site was most common in both cohorts, and most implants were placed in the submuscular location. In the Primary Augmentation Cohort, 19.7% of the breasts had a concomitant procedure with Mastopexy being the most common. More breasts in the Revision Augmentation Cohort underwent a concomitant breast procedure (74.8%), as expected, with 81.2% of those subjects having a Capsular Procedure. All available sizes of the IDEAL IMPLANT were used during the clinical trial.

Overall, there were 456 subjects (912 implants) who initially received the final version (8mm valve attachment component) of the device bilaterally, and 5 subjects (5 implants) who initially received the final version of the device unilaterally. For the Primary Augmentation Cohort, 363 subjects were initially implanted with bilateral 8mm valve attachment component implants (355 had slit baffle perforations; 8 had hole baffle perforations), 31 subjects initially received bilateral 6.3mm component implants (all had slit baffle perforations), and 5 subjects received a 6.3mm component implant on one side and a 8mm component implant on the other side (all had slit baffle perforations). A total of 391 subjects received slit baffle perforation implants and 11 received hole baffle perforation implants.

For the Revision Augmentation Cohort, 93 subjects were initially implanted with bilateral 8mm valve attachment component implants (90 had slit baffle perforations; 3 had hole baffle perforations), and 10 subjects received bilateral 6.3mm component implants (all slit baffle perforations). A total of 100 subjects received slit baffle perforation implants and 3 subjects received hole baffle perforation implants.

**Table 11**: Surgical Operative Data, per Implant

| Measure | Primary Augmentation (N=798) | Revision Augmentation (N=206) |
|---|---|---|
| Diameter valve attachment | | |
| 8mm | 91.6% (731/798) | 90.3% (186/206) |
| 6.3mm | 8.4% (67/798) | 9.7% (20/206) |
| Baffle perforation | | |
| Slits | 98.0% (782/798) | 97.1% (200/206) |
| Holes | 2.0% (16/798) | 2.9% (6/206) |
| Incision Site | | |
| Inframammary [1] | 70.8% (565/798) | 61.2% (126/206) |
| Periareolar | 22.2% (177/798) | 37.9% (78/206) |
| Axillary | 7.0% (56/798) | 1.0% (2/206) |
| Location | | |
| Subglandular | 8.0% (64/798) | 19.4% (40/206) |
| Submuscular | 92.0% (734/798) | 80.6% (166/206) |
| Concurrent breast procedure | | |
| Capsule procedure | 0% (0/157) | 81.2% (125/154) |

| | | |
|---|---|---|
| Mastopexy | 91.7% (144/157) | 26.0% (40/154) |
| Other | 8.3% (13/157) | 18.8% (29/154) |

Numbers are Mean ± SD (N), Median [Min, Max] for continuous measures and Percent (Count/N) for discrete measures.

[1] Two subjects each had two devices implanted via abdominoplasty and are reported as inframammary due to the approach used.

## D. Safety and Effectiveness Results

### 1. Safety Results

The analysis of safety was based on 399 subjects in the Primary Augmentation Cohort and 103 subjects in the Revision Augmentation Cohort.

#### a. Complication Rates

Table 12 shows the 2-year Kaplan-Meier (KM) risk rates of the first occurrence (95% confidence intervals) of adverse events for the two study cohorts per subject through 2 years. In the Primary Augmentation Cohort, complications occurring at a rate of ≥ 5% through 2 years included: all subsequent breast operations (14.2%) and implant removal with or without replacement (7.5%). In the Revision Cohort, complications occurring at a rate of ≥ 5% through 2 years included: all subsequent breast operations (23.7%), implant removal with or without replacement (15.1%), wrinkling/scalloping (12.0%), dissatisfaction with cosmetic results (8.9%), and capsular contracture – Grade III/IV (8.2%).

**Table 12:** KM Risk Rates of the First Occurrence of Adverse Events through 2 Years, per Subject

| Event (Includes all levels of severity) | Primary Augmentation (N=399) | Revision Augmentation (N=103) |
|---|---|---|
| Any complication or reoperation* | 42.2%**** (37.3%, 47.5%) | 50.5%**** (40.9%, 61.0%) |
| Any breast complication or reoperation* | 34.2%**** (29.5%, 39.3%) | 45.2%**** (35.7%, 55.8%) |
| All subsequent breast operations* | 14.2% (11.0%, 18.3%) | 23.7% (16.3%, 33.7%) |
| Related to implant | 8.4% (6.1%, 11.7%) | 11.1% (6.3%, 19.2%) |
| Related to procedure | 4.1% (2.5%, 6.6%) | 3.0% (1.0%, 9.0%) |
| Related to dissatisfaction with implant size | 2.3% (1.2%, 4.4%) | 4.0% (1.5%, 10.2%) |
| Other reason** | 6.9% (4.8%, 9.9%) | 15.7% (9.9%, 24.4%) |

| Event<br>(Includes all levels of severity) | Primary Augmentation<br>(N=399) | Revision Augmentation<br>(N=103) |
|---|---|---|
| Implant removal with or without replacement* | 7.5%<br>(5.2%, 10.8%) | 15.1%<br>(9.2%, 24.2%) |
| Anesthesia complications | 0.0% | 1.0%<br>(0.1%, 6.7%) |
| Neurologic complications | 0.3%<br>(0.0%, 1.8%) | 0.0% |
| Connective Tissue Disease diagnosis | 0.5%<br>(0.1%, 2.1%) | 0.0% |
| Reproductive problem | 0.5%<br>(0.1%, 2.1%) | 0.0% |
| Other Adverse event*** | 10.8%<br>(8.1%, 14.3%) | 14.0%<br>(8.6%, 22.6%) |
| Capsule contracture Grade II/III/IV | 17.1%<br>(13.7%, 21.2%) | 24.3%<br>(17.0%, 34.0%) |
| Capsule contracture Grade II | 14.0%<br>(10.9%, 17.8%) | 21.3%<br>(14.4%, 30.7%) |
| Capsule contracture Grade III | 3.6%<br>(2.1%, 5.9%) | 2.1%<br>(0.5%, 8.1%) |
| Capsule contracture Grade IV | 0.3%<br>(0.0%, 1.8%) | 2.1%<br>(0.5%, 8.1%) |
| Capsule contracture Grade III/IV | 3.8%<br>(2.3%, 6.3%) | 8.2%<br>(4.2%, 15.8%) |
| Wrinkling/scalloping (excludes mild severity) | 3.8%<br>(2.3%, 6.3%) | 12.0%<br>(7.0%, 20.2%) |
| Spontaneous deflation* | 4.8%<br>(3.0%, 7.6%) | 3.3%<br>(1.1%, 10.0%) |
| Seroma | 0.3%<br>(0.0%, 1.8%) | 2.9%<br>(0.9%, 8.8%) |
| Breast tissue atrophy/ chest wall deformity | 0.3%<br>(0.0%, 1.8%) | 0.0% |
| Dissatisfaction with cosmetic results | 4.1%<br>(2.5%, 6.6%) | 8.9%<br>(4.7%, 16.5%) |
| Hematoma/bleeding | 1.8%<br>(0.8%, 3.6%) | 0.0% |
| Wound healing delay/tissue necrosis/dehiscence | 1.3%<br>(0.5%, 3.0%) | 1.0%<br>(0.1%, 6.7%) |
| Wound infection | 1.3%<br>(0.5%, 3.0%) | 1.0%<br>(0.1%, 7.0%) |
| Implant exposure/extrusion | 0.0% | 2.0%<br>(0.5%, 7.8%) |
| Skin scar unsatisfactory | 1.5%<br>(0.7%, 3.4%) | 3.9%<br>(1.5%, 10.1%) |
| Mastopexy unsatisfactory | 1.5%<br>(0.7%, 3.4%) | 0.0% |
| Implant position unsatisfactory (malposition) | 2.6%<br>(1.4%, 4.7%) | 1.0%<br>(0.1%, 6.7%) |
| Persistent breast pain | 0.3%<br>(0.0%, 1.8%) | 1.1%<br>(0.1%, 7.2%) |

| Event (Includes all levels of severity) | Primary Augmentation (N=399) | Revision Augmentation (N=103) |
|---|---|---|
| Mastitis not requiring treatment | 0.5% (0.1%, 2.1%) | 0.0% |
| Inadequate milk supply | 0.3% (0.0%, 1.8%) | 1.1% (0.2%, 7.3%) |
| Lymphadenopathy | 0.3% (0.0%, 1.8%) | 0.0% |
| Dissatisfaction with implant size selected | 3.0% (1.7%, 5.3%) | 3.9% (1.5%, 10.1%) |
| Breast ptosis – after implant procedure | 0.5% (0.1%, 2.0%) | 4.1% (1.5%, 10.4%) |
| Breast lesion – benign | 1.5% (0.7%, 3.4%) | 4.1% (1.6%, 10.5%) |
| Breast lesion - malignant | 0.5% (0.1%, 2.0%) | 0.0% |

Numbers are failure rate determined by 1 – KM event-free rate.
* KM rates for Subsequent breast operation, Implant removal and Spontaneous deflation are based upon analyses of subjects with initial bilateral 8mm valve attachment component implants, N=363 for Primary Augmentation Cohort and N=93 for Revision Augmentation Cohort.
**Other reasons for subsequent breast operations: For the Primary Augmentation Cohort: breast ptosis, breast lesion, inadequate saline volume, dissatisfaction with cosmetic result and tubular breast; for the Revision Augmentation Cohort: inadequate saline volume, absence of implant, dissatisfaction with cosmetic result.
***Other adverse events: For the Primary Augmentation Cohort: nasal polyps, seizure disorder, bowel obstruction, hemorrhoids, hypothyroidism, emotional issue, neck rash, abdominal muscle bleed, rotator cuff problem, cholecystitis, foot fracture, contact dermatitis, back pain, tubular breast, liver cyst, herpes zoster infection, staph infection nose, anxiety, cystitis, diabetes, depression, head trauma, urinary retention, drug overdose, borderline personality disorder, anal fissure, arm cyst, abdominal incision pain, cold, herniated disc, enlarged thymus, kidney infection, rectal prolapse, abdominal wound infection, arm pain, sinus infection, nausea, eczema arms and renal stone. For the Revision Augmentation Cohort: sebaceous cysts of scalp, sinus obstruction, renal stone, seroma to abdomen, abdominal wound infection, anemia, femoral hernia, hand numbness, stasis ulcer ankle, superficial burn, intra-arterial septal communication, rash abdomen, EKG abnormality, back pain, diverticulitis, whooping cough and knee trauma.
**** 151 Primary Augmentation patients and 47 Revision Augmentation patients experienced at least one complication or reoperation through 2 years. 123 Primary Augmentation patients and 42 Revision Augmentation patients experienced at least one breast complication or reoperation through 2 years.

### b. Reasons for Subsequent Breast Operations

There were 97 total subsequent breast operations including 63 in the primary augmentation cohort and 34 in the revision augmentation cohort. Table 13 shows the reasons for subsequent breast operations stratified by cohort through 2 years.

The rates are based upon the total number of subsequent breast operations in subjects with initial bilateral 8mm valve attachment component implants.

**Table 13:** Reasons for Subsequent Breast Operations through 2 Years, Per Operation

| Reason Category | Reason | Primary Augmentation | Revision Augmentation |
|---|---|---|---|
| Implant-related | Capsular contracture (II) | 4.8% (3/63) | 2.9% (1/34) |
| | Capsular contracture (III-IV) | 7.9% (5/63) | 2.9% (1/34) |
| | Wrinkling/scalloping | 4.8% (3/63) | 11.8% (4/34) |
| | Spontaneous deflation (includes inner or outer lumen) | 25.4% (16/63) | 11.8% (4/34) |
| | Wide sternum anatomically | 1.6% (1/63) | 0.0% |
| Procedure - related | Hematoma/bleeding | 4.8% (3/63) | 0.0% |
| | Wound healing delay / Necrosis/dehiscence (no exposure) | 3.2% (2/63) | 0.0% |
| | Infection | 0.0% | 5.9% (2/34) |
| | Implant exposure/extrusion | 0.0% | 23.5% (8/34) |
| | Skin Scar Unsatisfactory | 3.2% (2/63) | 0.0% |
| | Mastopexy unsatisfactory | 4.8% (3/63) | 0.0% |
| | Implant position unsatisfactory (malposition) | 7.9% (5/63) | 0.0% |
| | Excess tissue breast fold | 1.6% (1/63) | 0.0% |
| | Stretched skin from ruptured silicone implant capsulectomy | 0.0% | 2.9% (1/34) |
| Dissatisfaction with size | Dissatisfaction with implant size (unilateral or bilateral) | 9.5% (6/63) | 11.8% (4/34) |
| Other reasons | Breast Ptosis prior to implant placement procedure | 3.2% (2/63) | 0.0% |
| | Breast Ptosis after implant placement procedure due to pregnancy, change in weight, and/or change in breast size | 1.6% (1/63) | 0.0% |
| | Breast Lesion – benign or malignant | 3.2% (2/63) | 0.0% |
| | Inadequate saline volume | 9.5% (6/63) | 14.7% (5/34) |
| | Absence of implant | 0.0% | 2.9% (1/34) |
| | Dissatisfaction with cosmetic result | 1.6% (1/63) | 8.8% (3/34) |
| | Tubular breast | 1.6% (1/63) | 0.0% |

Numbers are Percent (Count/N).

Denominator is the number of subsequent breast operations prior to the upper end of the visit window. One primary reason is summarized per operation.
If both implants were operated on and had different reasons, the primary reason will be selected following the reasons matching the collected categories as close as possible to the FDA guideline hierarchy.
Operation number is based upon analyses of subjects with initial bilateral final design of the implants: N=363 for Primary Augmentation Cohort and N=93 for Revision Augmentation Cohort.

Table 14 provides a breakdown of the types of surgical procedures that were performed through 2 years after implantation. Through 2 years, there were 51 Primary Augmentation patients who had one or more additional operations after the initial implantation (subsequent breast operations), for a total of 63 subsequent breast operations. These subsequent breast operations involved one or more surgical procedures for a total of 114 surgical procedures. Through 2 years, there were 22 Revision Augmentation patients who had one or more additional operations after the initial implantation (subsequent breast operations), for a total of 34 subsequent breast operations. These subsequent breast operations involved one or more surgical procedures for a total of 62 surgical procedures. Examples of multiple procedures during a single subsequent breast operation include implant replacement for both breasts or a capsule procedure and mastopexy on the same breast.

**Table 14:** Types of Subsequent Surgical Procedures through 2 Years, Per Procedure

| Procedure | Primary Augmentation N=114 | Revision Augmentation N=62 |
|---|---|---|
| Capsule procedure (e.g., release, excision, plasty) | 10.5% (12/114) | 19.4% (12/62) |
| Reposition a malpositioned implant | 6.1% (7/114) | 0.0% (0/62) |
| Explantation | | |
| No immediate replacement with any implant | 0.9% (1/114) | 8.1% (5/62) |
| With replacement using new IDEAL IMPANT | 23.7% (27/114) | 11.3% (7/62) |
| With replacement using other manufacturer implant | 14.0% (16/114) | 22.6% (14/62) |
| Evacuate hematoma/control bleeding | 2.6% (3/114) | 0.0% (0/62) |
| I&D and/or debridement | 0.9% (1/114) | 0.0% (0/62) |
| Skin scar revision and/or secondary would closure | 2.6% (3/114) | 3.2% (2/62) |
| Mastopexy – primary or revision | 14.0% (16/114) | 1.6% (1/62) |
| Treatment of breast lesion (e.g., open biopsy, lumpectomy) | 1.8% (2/114) | 0.0% (0/62) |
| Fill volume adjustments | 19.3% (22/114) | 24.2% (15/62) |
| Other | 3.5% (4/114)* | 9.7% (6/62)** |

Based upon analyses of subjects with initial bilateral final design of the implants: N=363 for Primary Augmentation Cohort and N=93 for Revision Augmentation

Cohort. Subsequent breast operations were performed in 51 primary augmentation patients and 22 revision augmentation patients.
* Mastectomy and fat grafting to breasts.
** Excise skin, fat transfer to breasts and replace implants.

### c. Reasons for Implant Removal

There were 70 total implants that were removed through 2 years, including 44 in the primary augmentation cohort and 26 in the revision augmentation cohort. Table 15 shows the reasons for implant removal stratified by cohort through 2 years. The rates are based upon the total number of implant removals in subjects with initial bilateral 8mm valve attachment component implants.

**Table 15:** Reasons for Implant Removal through 2 Years, Per Implant

| Reason Category | Reason | Primary Augmentation | Revision Augmentation |
|---|---|---|---|
| Implant-related | Capsular contracture (II) | 2.3% (1/44) | 3.8% (1/26) |
| | Capsular contracture (III-IV) | 6.8% (3/44) | 3.8% (1/26) |
| | Wrinkling/scalloping | 2.3% (1/44) | 7.7% (2/26) |
| | Spontaneous deflation (includes inner or outer lumen) | 36.4% (16/44) | 19.2% (5/26) |
| Procedure - related | Healing delay / Necrosis /dehiscence (no exposure) | 2.3% (1/44) | 0.0% |
| | Infection | 0.0% | 3.8% (1/26) |
| | Implant exposure/extrusion | 0.0% | 15.4% (4/26) |
| Dissatisfaction with size | Dissatisfaction with implant size (unilateral or bilateral) | 29.5% (13/44) | 23.1% (6/26) |
| Other | Breast Lesion – benign or malignant | 2.3% (1/44) | 0.0% |
| | Dissatisfaction with cosmetic result | 4.5% (2/44) | 23.1% (6/26) |
| | Replaced to match other implant | 11.4% (5/44) | 0.0% |
| | Preventive mastectomy | 2.3% (1/44) | 0.0% |

Numbers are Percent (Count/N).
Denominator is the number of implants removed (with or without replacement). Implants were removed from 27 primary augmentation patients and from 14 revision augmentation patients.
Based upon analyses of subjects with initial bilateral final design of the implants: N=363 for Primary Augmentation Cohort and N=93 for Revision Augmentation Cohort.

Among the Primary Augmentation patients, there were 28 implants removed and replaced with IDEAL IMPLANTS. Table 16 below reflects the number of replaced implants (not patients) out of 100 implants associated with the listed complications following replacement. For example there was wound infection in approximately 4% or 4 out of 100 Primary Augmentation implants at some time within 2 years after replacement. Among the Revision Augmentation patients, there were 9 implants removed and replaced with IDEAL IMPLANTS. The table below reflects the number of replaced implants (not patients) out of 100 implants associated with the listed complications within 2 years following replacement. For example there was capsular contracture in 11% or 11 out of 100 Revision Augmentation implants at some time within 2 years after replacement. There were no new adverse events reported among patients who had their implants removed and not replaced.

**Table 16:** New Adverse Events after Removal of IDEAL IMPLANT and Replacement with IDEAL IMPLANT, per Implant

| Event | Primary Augmentation | Revision Augmentation |
|---|---|---|
| Capsule contracture Grade II/III/IV | 0.0% (0/28) | 11.1% (1/9) |
| Wrinkling/scalloping | 0.0% (0/28) | 11.1% (1/9) |
| Dissatisfaction with cosmetic results | 0.0% (0/28) | 11.1% (1/9) |
| Wound infection | 3.6% (1/28) | 11.1% (1/9) |
| Implant exposure/extrusion | 0.0% (0/28) | 11.1% (1/9) |
| Subsequent breast operation | 7.1% (2/28) | 22.2% (2/19) |

Based upon analyses of subjects with initial bilateral final design of the implants: N=363 for Primary Augmentation Cohort and N=93 for
Revision Augmentation Cohort.

**d. Other Clinical Safety Outcomes**

This section summarizes post-implant observations pertaining to breast disease, connective tissue disease (CTD), lactation and reproduction problems, anaplastic large cell lymphoma (ALCL) and suicide. These data should be interpreted with caution in that there was no comparison group of similar women without implants. Confirmed reports were based on a diagnosis by a physician.

Breast Disease

In the Primary Augmentation Cohort, there were 4 reports of abnormal mammogram findings: 1 breast cancer at 3 months post implantation, 1 breast mass at 8 months, 1 calcification at 9 months and 1 additional evaluation necessary at 2 months. In the Revision Augmentation Cohort, there were 3 reports of abnormal mammogram findings: 1 cyst at 11 months post

implantation, 1 calcification at 4 months and 1 additional evaluation necessary at 7 months.

Connective Tissue/Autoimmune Disease (CTD)
Subjects underwent a screening for connective tissue disorders at each follow-up visit. Approximately 1% (N=5) of the subjects in the Primary Augmentation Cohort and 5% (N=5) of the subjects in the Revision Augmentation Cohort were referred to a board certified Rheumatologist at the 2 year visit. A diagnosis of CTD was made in 2 patients in the Primary Augmentation Cohort: one with lupus at 13 months post implantation and one with non-specific arthritis at 24 months post implantation. No patient in the Revision Augmentation Cohort was diagnosed with a CTD.

Lactation and Reproduction Problems
In the Primary Augmentation Cohort, 3 patients experienced lactation complications: 2 had mastitis at 19 and 24 months post implantation; 1 had inadequate milk production at 11 months. In the Revision Augmentation Cohort, 1 patient experienced inadequate milk production at 24 months post implantation. In the Primary Augmentation Cohort, 3 patients had a reproductive problem (miscarriage) at 10, 22, and 23 months post implantation. No patient in the Revision Augmentation Cohort experienced a reproductive problem.

Anaplastic Large Cell Lymphoma
Through 2 years, there were no reports of anaplastic large cell lymphoma (ALCL) in any of the patient cohorts.

Suicide
There were no reports of suicide in either cohort through 2 years.

**e. Other Safety Endpoints**

The clinical protocol specified that subjects were to undergo an evaluation at each follow-up visit for capsular contracture using the Baker Classification. Table 17 shows capsular contracture per implant.

**Table 17:** Capsular Contracture Class at Each Follow-up Visit, per Implant

| Cohort | Class | 2 mo | 6 mo | 1 yr | 2yrs |
|---|---|---|---|---|---|
| Primary Augmentation | I | 94.3% (749/794) | 95.9% (746/778) | 96.5% (739/766) | 94.8% (713/752) |
| | II | 5.2% (41/794) | 2.8% (22/778) | 2.6% (20/766) | 3.9% (29/752) |
| | III | 0.5% (4/794) | 1.2% (9/778) | 0.9% (7/766) | 1.3% (10/752) |
| | IV | 0.0% (0/794) | 0.1% (1/778) | 0.0% (0/766) | 0.0% (0/752) |

| | | | | | |
|---|---|---|---|---|---|
| Revision Augmentation | I | 96.1% (197/205) | 94.0% (188/200) | 92.1% (175/190) | 90.9% (170/187) |
| | II | 3.9% (8/205) | 5.0% (10/200) | 6.3% (12/190) | 5.9% (11/187) |
| | III | 0.0% (0/205) | 1.0% (2/200) | 1.1% (2/190) | 2.7% (5/187) |
| | IV | 0.0% (0/205) | 0.0% (0/200) | 0.5% (1/190) | 0.5% (1/187) |

Numbers are Percent (Count/N).
Severity of ongoing capsular contracture adverse events was recorded at each subsequent follow-up visit. Therefore, counts by follow-up visit may not match incidence rates for capsular contracture adverse events, which include only new onset events in the given time frame.

### f. Cumulative Risk for Occurrence of Each Adverse Event at Each Follow-up Visit

Table 18 shows the KM rate for the first occurrence for each complication at each follow-up visit.

**Table 18:** Kaplan-Meier Rates for Adverse Events by Time Point, per Subject

| Event (Includes all levels of severity) | Primary Augmentation (N= 399) | | | | Revision Augmentation (N=103) | | | |
|---|---|---|---|---|---|---|---|---|
| | 2 mo | 6 mo | 1 yr | 2 yr | 2 mo | 6 mo | 1 yr | 2 yr |
| Any complication or reoperation* | 19.1% (15.4%, 23.6%) | 29.4% (25.0%, 34.4%) | 35.3% (30.6%, 40.5%) | 42.2% (37.3%, 47.5%) | 23.7% (16.3%, 33.7%) | 36.6% (27.7%, 47.2%) | 44.1% (34.7%, 54.8%) | 50.5% (40.9%, 61.0%) |
| Any breast complication or reoperation* | 15.4% (12.1%, 19.6%) | 24.0% (19.9% 28.7%) | 27.9% (23.6%, 32.9%) | 34.2% (29.5%, 39.3%) | 19.4% (12.7%, 28.9%) | 31.2% (22.8%, 41.7%) | 37.6% (28.7%, 48.3%) | 45.2% (35.7%, 55.8%) |
| All subsequent breast operations* | 1.7% (0.7%, 3.6%) | 5.0% (3.2%, 7.8%) | 11.1% (8.3%, 14.8%) | 14.2% (11.0%, 18.3%) | 1.1% (0.2%, 7.4%) | 15.1% (9.2%, 24.1%) | 18.3% (11.8%, 27.7%) | 23.7% (16.3%, 33.7%) |
| Related to implant | 0.5% (0.1%, 2.0%) | 2.0% (1.0%, 4.0%) | 5.1% (3.3%, 7.8%) | 8.4% (6.1%, 11.7%) | 1.0% (0.1%, 6.7%) | 2.9% (1.0%, 8.8%) | 7.0% (3.4%, 14.2%) | 11.1% (6.3%, 19.2%) |
| Related to procedure | 1.0% (0.4%, 2.6%) | 2.0% (1.0%, 4.0%) | 3.6% (2.1%, 5.9%) | 4.1% (2.5%, 6.6%) | 0.0% | 2.0% (0.5%, 7.7%) | 3.0% (1.0%, 9.0%) | 3.0% (1.0%, 9.0%) |
| Related to dissatisfaction with implant size | 0.3% (0.0%, 1.8%) | 0.8% (0.2%, 2.3%) | 2.0% (1.0%, 4.0%) | 2.3% (1.2%, 4.4%) | 0.0% | 4.0% (1.5%, 10.2%) | 4.0% (1.5%, 10.2%) | 4.0% (1.5%, 10.2%) |
| Other reason** | 0.5% (0.1%, 2.0%) | 2.8% (1.5%, 4.9%) | 4.8% (3.1%, 7.4%) | 6.9% (4.8%, 9.9%) | 1.0% (0.1%, 6.7%) | 11.7% (6.8%, 19.6%) | 13.7% (8.3%, 22.0%) | 15.7% (9.9%, 24.4%) |
| Implant removal with or without replacement* | 0.6% (0.1%, 2.2%) | 2.5% (1.3%, 4.7%) | 4.7% (3.0%, 7.5%) | 7.5% (5.2%, 10.8%) | 0.0% | 7.5% (3.7%, 15.1%) | 10.8% (5.9%, 19.1%) | 15.1% (9.2%, 24.2%) |
| Anesthesia complications | 0.0% | 0.0% | 0.0% | 0.0% | 1.0% (0.1%, 6.7%) | 1.0% (0.1%, 6.7%) | 1.0% (0.1%, 6.7%) | 1.0% (0.1%, 6.7%) |
| Neurologic complications | 0.3% (0.0%, 1.8%) | 0.3% (0.0%, 1.8%) | 0.3% (0.0%, 1.8%) | 0.3% (0.0%, 1.8%) | 0.0% | 0.0% | 0.0% | 0.0% |

| Event (Includes all levels of severity) | Primary Augmentation (N= 399) | | | | Revision Augmentation (N=103) | | | |
|---|---|---|---|---|---|---|---|---|
| | 2 mo | 6 mo | 1 yr | 2 yr | 2 mo | 6 mo | 1 yr | 2 yr |
| Connective Tissue Disease diagnosis | 0.0% | 0.0% | 0.0% | 0.5% (0.1%, 2.1%) | 0.0% | 0.0% | 0.0% | 0.0% |
| Reproductive problem | 0.0% | 0.0% | 0.0% | 0.5% (0.1%, 2.1%) | 0.0% | 0.0% | 0.0% | 0.0% |
| Other Adverse Event*** | 3.5% (2.1%, 5.9%) | 5.3% (3.5%, 8.0%) | 7.9% (5.6%, 11.0%) | 10.8% (8.1%, 14.3%) | 6.8% (3.3%, 13.7%) | 7.8% (4.0%, 15.0%) | 10.9% (6.2%, 18.8%) | 14.0% (8.6%, 22.6%) |
| Capsule contracture Grade II/III/IV | 7.8% (5.5%, 10.9%) | 11.3% (8.6%, 14.9%) | 13.4% (10.4%, 17.1%) | 17.1% (13.7%, 21.2%) | 5.8% (2.7%, 12.5%) | 11.8% (6.9%, 19.9%) | 18.0% (11.7%, 27.0%) | 24.3% (17.0%, 34.0%) |
| Capsule contracture Grade II | 6.5% (4.5%, 9.4%) | 9.0% (6.6%, 12.3%) | 10.9% (8.2%, 14.4%) | 14.0% (10.9%, 17.8%) | 5.8% (2.7%, 12.5%) | 9.9% (5.4%, 17.5%) | 16.0% (10.1%, 24.8%) | 21.3% (14.4%, 30.7%) |
| Capsule contracture Grade III | 1.5% (0.7%, 3.3%) | 2.3% (1.2%, 4.3%) | 2.8% (1.5%, 5.0%) | 3.6% (2.1%, 5.9%) | 0.0% | 2.0% (0.5%, 7.6%) | 4.0% (1.5%, 10.3%) | 8.2% (4.2%, 15.8%) |
| Capsule contracture Grade IV | 0.0% | 0.3% (0.0%, 1.8%) | 0.3% (0.0%, 1.8%) | 0.3% (0.0%, 1.8%) | 0.0% | 0.0% | 1.0% (0.1%, 7.0%) | 2.1% (0.5%, 8.1%) |
| Capsule contracture Grade III/IV | 1.5% (0.7%, 3.3%) | 2.5% (1.4%, 4.6%) | 3.0% (1.7%, 5.3%) | 3.8% (2.3%, 6.3%) | 0.0% | 2.0% (0.5%, 7.6%) | 4.0% (1.5%, 10.3%) | 8.2% (4.2%, 15.8%) |
| Wrinkling/scalloping (excludes mild severity) | 0.5% (0.1%, 2.0%) | 1.8% (0.8%, 3.7%) | 3.0% (1.7%, 5.3%) | 3.8% (2.3%, 6.3%) | 2.9% (0.9%, 8.8%) | 6.9% (3.3%, 13.8%) | 9.9% (5.5%, 17.7%) | 12.0% (7.0%, 20.2%) |
| Spontaneous deflation* | 0.3% (0.0%, 1.9%) | 1.4% (0.6%, 3.3%) | 2.2% (1.1%, 4.4%) | 4.8% (3.0%, 7.6%) | 1.1% (0.2%, 7.4%) | 2.2% (0.5%, 8.4%) | 2.2% (0.5%, 8.4%) | 3.3% (1.1%, 10.0%) |
| Seroma | 0.3% (0.0%, 1.8%) | 0.3% (0.0%, 1.8%) | 0.3% (0.0%, 1.8%) | 0.3% (0.0%, 1.8%) | 2.9% (0.9%, 8.8%) | 2.9% (0.9%, 8.8%) | 2.9% (0.9%, 8.8%) | 2.9% (0.9%, 8.8%) |
| Breast tissue atrophy/chest wall deformity | 0.0% | 0.3% (0.0%, 1.8%) | 0.3% (0.0%, 1.8%) | 0.3% (0.0%, 1.8%) | 0.0% | 0.0% | 0.0% | 0.0% |
| Dissatisfaction with cosmetic results | 1.3% (0.5%, 3.0%) | 2.0% (1.0%, 4.0%) | 2.3% (1.2%, 4.3%) | 4.1% (2.5%, 6.6%) | 2.9% (0.9%, 8.8%) | 4.9% (2.0%, 11.3%) | 6.9% (3.3%, 13.8%) | 8.9% (4.7%, 16.5%) |
| Hematoma/bleeding | 1.5% (0.7%, 3.3%) | 1.8% (0.8%, 3.6%) | 1.8% (0.8%, 3.6%) | 1.8% (0.8%, 3.6%) | 0.0% | 0.0% | 0.0% | 0.0% |
| Wound healing delay/tissue necrosis/dehiscence | 1.0% (0.4%, 2.6%) | 1.3% (0.5%, 3.0%) | 1.3% (0.5%, 3.0%) | 1.3% (0.5%, 3.0%) | 1.0% (0.1%, 6.7%) | 1.0% (0.1%, 6.7%) | 1.0% (0.1%, 6.7%) | 1.0% (0.1%, 6.7%) |
| Wound infection | 0.5% (0.1%, 2.0%) | 1.0% (0.4%, 2.7%) | 1.3% (0.5%, 3.0%) | 1.3% (0.5%, 3.0%) | 0.0% | 0.0% | 1.0% (0.1%, 7.0%) | 1.0% (0.1%, 7.0%) |
| Implant exposure/extrusion | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% | 1.0% (0.1%, 6.8%) | 2.0% (0.5%, 7.8%) | 2.0% (0.5%, 7.8%) |
| Skin scar unsatisfactory | 0.8% (0.2%, 2.3%) | 1.0% (0.4%, 2.7%) | 1.0% (0.4%, 2.7%) | 1.5% (0.7%, 3.4%) | 1.9% (0.5%, 7.5%) | 3.9% (1.5%, 10.1%) | 3.9% (1.5%, 10.1%) | 3.9% (1.5%, 10.1%) |
| Mastopexy unsatisfactory | 0.8% (0.2%, 2.3%) | 1.0% (0.4%, 2.7%) | 1.0% (0.4%, 2.7%) | 1.5% (0.7%, 3.4%) | 0.0% | 0.0% | 0.0% | 0.0% |

| Event (Includes all levels of severity) | Primary Augmentation (N= 399) | | | | Revision Augmentation (N=103) | | | |
|---|---|---|---|---|---|---|---|---|
| | 2 mo | 6 mo | 1 yr | 2 yr | 2 mo | 6 mo | 1 yr | 2 yr |
| Implant position unsatisfactory (malposition) | 0.5% (0.1%, 2.0%) | 1.3% (0.5%, 3.0%) | 1.5% (0.7%, 3.3%) | 2.6% (1.4%, 4.7%) | 1.0% (0.1%, 6.7%) | 1.0% (0.1%, 6.7%) | 1.0% (0.1%, 6.7%) | 1.0% (0.1%, 6.7%) |
| Persistent breast pain | 0.3% (0.0%, 1.8%) | 0.3% (0.0%, 1.8%) | 0.3% (0.0%, 1.8%) | 0.3% (0.0%, 1.8%) | 0.0% | 0.0% | 0.0% | 1.1% (0.1%, 7.2%) |
| Mastitis not requiring treatment | 0.0% | 0.0% | 0.0% | 0.5% (0.1%, 2.1%) | 0.0% | 0.0% | 0.0% | 0.0% |
| Inadequate milk supply | 0.0% | 0.0% | 0.3% (0.0%, 1.8%) | 0.3% (0.0%, 1.8%) | 0.0% | 0.0% | 0.0% | 1.1% (0.2%, 7.3%) |
| Lymphadenopathy | 0.3% (0.0%, 1.8%) | 0.3% (0.0%, 1.8%) | 0.3% (0.0%, 1.8%) | 0.3% (0.0%, 1.8%) | 0.0% | 0.0% | 0.0% | 0.0% |
| Dissatisfaction with implant size selected | 1.3% (0.5%, 3.0%) | 2.8% (1.5%, 4.9%) | 3.0% (1.7%, 5.3%) | 3.0% (1.7%, 5.3%) | 1.9% (0.5%, 7.5%) | 3.9% (1.5%, 10.1%) | 3.9% (1.5%, 10.1%) | 3.9% (1.5%, 10.1%) |
| Breast ptosis - after implant procedure | 0.0% | 0.3% (0.0%, 1.8%) | 0.3% (0.0%, 1.8%) | 0.5% (0.1%, 2.0%) | 0.0% | 1.0% (0.1%, 6.8%) | 2.0% (0.5%, 7.8%) | 4.1% (1.5%, 10.4%) |
| Breast lesion - benign | 0.0% | 0.5% (0.1%, 2.0%) | 0.8% (0.2%, 2.3%) | 1.5% (0.7%, 3.4%) | 0.0% | 1.0% (0.1%, 6.8%) | 3.0% (1.0%, 9.1%) | 4.1% (1.6%, 10.5%) |
| Breast lesion - malignant | 0.0% | 0.5% (0.1%, 2.0%) | 0.5% (0.1%, 2.0%) | 0.5% (0.1%, 2.0%) | 0.0% | 0.0% | 0.0% | 0.0% |

Numbers are failure rate determined by 1 - Kaplan Meier event-free rate. Subjects who remain in the study through 2 years and are event
free at their most recent follow-up are assumed to be event free at the upper end of the 2-year visit window.

* KM rates for these Subsequent breast operation, Implant removal and Spontaneous deflation are based upon analyses of subjects with initial bilateral final design of valve attachment component implants, N=363 for Primary Augmentation Cohort and N=93 for Revision Augmentation Cohort.

**Other reasons for subsequent breast operations: For the Primary Augmentation Cohort: breast ptosis, breast lesion, inadequate saline volume, dissatisfaction with cosmetic result and tubular breast; for the Revision Augmentation Cohort: inadequate saline volume, absence of implant, dissatisfaction with cosmetic result.

***Other adverse events: For the Primary Augmentation Cohort: nasal polyps, seizure disorder, bowel obstruction, hemorrhoids, hypothyroidism, emotional issue, neck rash, abdominal muscle bleed, rotator cuff problem, cholecystitis, foot fracture, contact dermatitis, back pain, tubular breast, liver cyst, herpes zoster infection, staph infection nose, anxiety, cystitis, diabetes, depression, head trauma, urinary retention, drug overdose, borderline personality disorder, anal fissure, arm cyst, abdominal incision pain, cold, herniated disc, enlarged thymus, kidney infection, rectal prolapse, abdominal wound infection, arm pain, sinus infection, nausea, eczema arms and renal stone. For the Revision Augmentation Cohort: sebaceous cysts of scalp, sinus obstruction, renal stone, seroma to abdomen, abdominal wound infection, anemia, femoral hernia, hand numbness, stasis ulcer ankle, superficial burn, intra-arterial septal communication, rash abdomen, EKG abnormality, back pain, diverticulitis, whooping cough and knee trauma.

## 2. Effectiveness Results

The analysis of effectiveness was based on the 502 evaluable patients at the 2 year time point. Key effectiveness outcomes are presented below.

### a. Increase in Breast Size

Increase in breast size from baseline was analyzed for subjects in the Primary Augmentation Cohort. As shown in Table 19, subjects experienced a mean increase of 2.5 inches in chest circumstance measurements (breast size).

**Table 19:** Increase in Breast Size (Inches) per Subject for the Primary Augmentation Cohort

| Chest Measurements | Primary Augmentation (N=391) |
|---|---|
| Baseline measurement (inches) | 3.6±1.4 (389)<br>3.5 [-2.0, 9.5] |
| 1-year measurement (inches) | 6.1±1.3 (375)<br>6.0 [2.0, 10.0] |
| Change from baseline at 1 year (inches) | 2.5±1.5 (374)<br>2.5 [-4.3, 6.5] |

Numbers are Mean ± SD (N), Median [Min, Max].
The measurement presented for each visit is the chest circumference at the nipples minus at the inframammary fold. The change is the difference in this measure between visits.
Eight patients were not included in the analysis because they were implanted with hole baffle perforation implants for which approval is not being sought.

### b. Breast Evaluation Questionnaire (BEQ)

The BEQ was utilized to assess subjects' satisfaction with their breasts before and after implant surgery. Subjects in the Primary Augmentation Cohort and the Revision Augmentation cohort experienced significant increases from baseline in each domain of the BEQ. These differences were all statistically significant for each domain at both 1 and 2 years (t-test; p-value <0.0001). At 2 years, subjects in the Primary Augmentation Cohort reported: a mean of 54.9 (60 maximum score possible) on the Comfort Fully Dressed scale, a mean increase of 14.2 compared to the baseline; a mean of 98.7 (120 maximum score possible) on the Comfort Not Fully Dressed scale, a mean increase of 43.4 compared to the baseline; and a mean of 39.8 (45 maximum score possible) on the Satisfaction with Breast Attributes scale, a mean increase of 18.4 compared to the baseline. Subjects in the Revision Augmentation Cohort reported: a mean of 54.2 on the Comfort Fully Dressed scale, a mean increase of 7.5 compared to the baseline; a mean of 93.2 on the Comfort Not Fully Dressed scale, a mean increase of 18.0 compared to the

baseline; and a mean of 39.1 on the Satisfaction with Breast Attributes scale, a mean increase of 8.7 compared to the baseline.

**c. Subject and Investigator Satisfaction with Outcome**

Subject and investigator satisfaction with the outcome achieved were assessed using a five-point Likert scale, which ranged from Definitely Dissatisfied to Definitely Satisfied. Satisfaction was assessed with the overall cosmetic outcome, which may have included concurrent breast procedures. Table 20 shows the results per implant. The investigators were satisfied with the implants' outcomes 95.9% (709/739) of the time at 2 years in the Primary Augmentation Cohort and 91.7% (166/181) of the time at 2 years in the Revision Augmentation Cohort. Subjects were equally satisfied. At 2 years, subjects were satisfied with the implants' outcomes 94.3% (697/739) and 90.6% (164/181) of the time in the Primary Augmentation Cohort and the Revision Augmentation Cohort, respectively.

**Table 20:** Investigator and Subject Satisfaction with Outcome, per Implant at 2 Years

| Satisfaction Group | Satisfaction Measure | 2-Year Follow-up Visit | |
|---|---|---|---|
| | | Primary Augmentation | Revision Augmentation |
| Physician Satisfaction | Definitely satisfied with outcome | 83.2% (615/739) | 77.9% (141/181) |
| | Somewhat satisfied with outcome with outcome | 12.7% (94/739) | 13.8% (25/181) |
| | Neither satisfied nor dissatisfied with outcome | 1.5% (11/739) | 2.8% (5/181) |
| | Somewhat dissatisfied with outcome | 1.9% (14/739) | 5.5% (10/181) |
| | Definitely dissatisfied with outcome | 0.7% (5/739) | 0% (0/181) |
| Subject Satisfaction | Definitely satisfied with outcome | 78.1% (577/739) | 76.2% (138/181) |
| | Somewhat satisfied with outcome with outcome | 16.2% (120/739) | 14.4% (26/181) |
| | Neither satisfied nor dissatisfied with outcome | 1.4% (10/739) | 2.8% (5/181) |
| | Somewhat dissatisfied with outcome | 2.8% (21/739) | 5.5% (10/181) |
| | Definitely dissatisfied with outcome | 1.5% (11/739) | 1.1% (2/181) |

Twenty-two implants were not included in the analysis because they were implanted with hole baffle perforation implants for which approval is not being sought. Data from 370 Primary Augmentation and 91 Revision Augmentation patients is included in the satisfaction analysis.

**d. SF-36 Scores**

The SF-36v2® Health Survey is a 36-item survey that captures patient reported health outcomes; it consists of 8 scales and psychometrically-based physical component summary (PCS) and mental component summary (MCS) scores. For all eight scales and at all time points the mean SF-36 scores were clinically

significantly higher for subjects compared to the general female population. Comparison of baseline scores to scores at 1 and 2 years show no clinically significant changes. There were a number of statistically significant decreases in certain quality of life scales. More importantly, these changes were small or very small and, therefore, are not considered to be clinically relevant. Similar findings have been reported in other clinical trials of breast implants where small decreases in certain SF-36 scores were noted.

### 3. Risk Factor Analysis

A multivariate analysis was performed to evaluate whether any demographic characteristics, surgical factors or implant size were associated with reported adverse events. One covariate was statistically associated with several adverse events: age. As age increased, there were small increases in risk for capsular contracture, all subsequent breast operations, implant-related subsequent operation and implant removal. Age is a well-known risk factor for many medical procedures. Although these findings were present, the effect of age was small in magnitude and judged not to be clinically relevant. Surgical incision site was associated with all subsequent breast operations and implant removal in the Primary Augmentation Cohort. Incision size, which was analyzed as a continuous variable, was associated with capsule contracture (Grade III and IV) and implant-related subsequent breast operations in the Primary Augmentation Cohort. In both analyses, there was a slight increase in risk of experiencing the adverse event (Grade III and IV capsule contracture or implant-related subsequent breast operation) with increasing incision size, but the magnitude of the effect was small. Implant size was associated with implant removal in the Revision Augmentation Cohort only. The effects of the risk factors were small in magnitude.

## E. Financial Disclosure

The Financial Disclosure by Clinical Investigators regulation (21 CFR 54) requires applicants who submit a marketing application to include certain information concerning the compensation to, and financial interests and arrangement of, any clinical investigator conducting clinical studies covered by the regulation. The pivotal clinical study included 35 investigators, of which 1 investigator was a full-time or part-time employees of the sponsor and 2 investigators, including the employee noted above, had disclosable financial interests/arrangements as defined in 21 CFR 54.2(a), (b), (c) and (f) and described below:

- Compensation to the investigator for conducting the study where the value could be influenced by the outcome of the study: 0 investigators
- Significant payment of other sorts: 0 investigators
- Proprietary interest in the product tested held by the investigator: 0 investigators

- Significant equity interest held by investigator in sponsor of covered study: 2 investigators

The applicant has adequately disclosed the financial interest/arrangements with clinical investigators. Statistical analyses were conducted by FDA to determine whether the financial interests/arrangements had any impact on the clinical study outcome. The information provided does not raise any questions about the reliability of the data.

## XI. PANEL MEETING RECOMMENDATION AND FDA'S POST-PANEL ACTION

In accordance with the provisions of section 515(c)(2) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the General and Plastic Surgery Advisory Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

## XII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

### A. Effectiveness Conclusions

The effectiveness outcomes demonstrate that the majority of patients who underwent a chest measurement (primary augmentation cohort only), report an increase in chest circumference. The majority of patients who provided Breast Evaluation Questionnaire assessments at the 1 and 2-year assessment point had favorable results. The majority of patients who provided a satisfaction rating at 2 years indicated that they were satisfied with their breast implants. The majority of physicians who provided a satisfaction rating at 2 years reported being satisfied with the breast implants. Comparison of baseline SF-36 scores to scores at 1 and 2 years show no clinically significant changes.

### B. Safety Conclusions

The risks of the device are based on nonclinical laboratory and/or animal studies as well as data collected in a clinical study conducted to support PMA approval as described above.

Cumulative risk of complication through 2-year follow-up demonstrated that 42.2% of primary augmentation patients experienced complications, and 50.5% of revision augmentation patients experienced complications. In addition, 34.2% of primary augmentation patients experienced breast related complications, and 45.2% of revision augmentation patients experienced breast related complications. The most common complications through 2 years were reoperations, implant removal with or without replacement, capsular contracture and wrinkling/scalloping.

### C. Benefit Risk Conclusions

The probable benefits of the device are also based on data collected in a clinical study conducted to support PMA approval as described above.

Additional factors to be considered in determining probable risks and benefits for the IDEAL IMPLANT® Saline-filled Breast Implant device included: the active and deliberate search/documentation of adverse events in the clinical study, single arm pivotal study design, lacking individual patient success criteria, good patient follow-up through 2 years, the availability of alternative treatments, patient-centric assessments, and risk mitigation with device use by trained surgeons in patients with informed consent.

In conclusion, given the available information above, the data support that the probable benefits outweigh the probable risks for women for IDEAL IMPLANT® Saline-filled Breast Implant for the following procedures:

- Primary breast augmentation to increase breast size.
- Revision breast augmentation to correct or improve the result of a primary breast augmentation surgery.

### D. Overall Conclusions

The data in this application support the reasonable assurance of safety and effectiveness of this device when used in accordance with the indications for use. The benefits and risks of breast implants are sufficiently well understood for women to make informed decisions about their use. The 2-year clinical results demonstrate that IDEAL IMPLANT® Saline-filled Breast Implants are reasonably safe and effective for use in primary augmentation and revision augmentation.

## XIII. CDRH DECISION

CDRH issued an approval order on November 14, 2014. The final conditions of approval cited in the approval order are described below.

The sponsor agrees to submit reports to the Office of Device Evaluation (ODE) under the PMA Annual Reports for the following:

1. Conduct a Focus Group Study to evaluate whether the IDEAL IMPLANT® Saline-filled Breast Implant for Breast Augmentation Surgery brochure effectively communicate the risks and benefits of breast implant surgery to women interested in primary or revision breast augmentation, according to the protocol version dated 3/18/14. Upon completion of the focus group study, you must submit a Final Report

of the Focus Group Study findings and suggested revision of patient and physician labeling based on those findings.

2. Conduct a Device Explant Analyses for all IDEAL IMPLANT Saline-filled Breast Implants that are retrieved, per explant analysis protocol version dated 7/7/14. On an annual basis, you must report the results of these Device Explant Analyses in the PMA Annual Reports.

In addition to the Annual Report requirements, the sponsor must provide the following data in post-approval study reports (PAS):

Post-Approval PMA Cohort Study (PACS): Per post-approval study protocol version dated February 27, 2014, this study will consist of the continued follow-up of the premarket cohort. Study participants will be followed annually for 10 years in order to assess the long-term clinical performance of their device. The Post-Approval PMA Cohort Study (PACS) will include a total of 502 subjects. The PACS data are to be collected via annual physician follow-up evaluations. All safety and effectiveness endpoints evaluated at premarket will continue to be studied long-term. The safety endpoints include all adverse events that will be collected throughout the study. Additionally, several distinct adverse events, including (but not limited to) peri-prosthetic infection, seroma, capsule contracture (Baker class II-IV), explant, spontaneous failure of inner shell, spontaneous failure of outer shell and spontaneous deflation, will be summarized separately. Summary statistics, including histograms, will be generated for all relevant variables. Both by-patient and by-implant analyses will be presented. Non-respondent bias will be assessed by comparing baseline characteristics of those patients that are lost to follow-up against those that are followed for the entirety of the study.

The sponsor must also update their patient and physician labeling to reflect 5 and 10-year PACS study findings on the safety and effectiveness of the device, as soon as these data are available, as well as any other time point deemed necessary by FDA if significantly new information from this study becomes available.

On an annual basis, the sponsor must submit a PACS progress report to FDA that includes: (1) the follow-up status of study subjects; and (2) a summary of findings for all study endpoints. The reports should clearly be identified as Post-Approval Study Report. Two copies for each study, identified as "PMA Post-Approval Study Report" and bearing the applicable PMA reference number, should be submitted to the address below. For more information on post-approval studies, see the FDA guidance document entitled, "Procedures for Handling Post-Approval Studies Imposed by PMA Order" (www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm070974.htm#2).

The sponsor also agrees to participate as a stakeholder in developing the National Breast Implants Registry.

The applicant's manufacturing facility has been inspected and found to be in compliance with the device Quality System (QS) regulation (21 CFR 820).

## XIV. APPROVAL SPECIFICATIONS

Directions for use: See device labeling.

Hazards to Health from Use of the Device: See Indications, Contraindications, Warnings, Precautions, and Adverse Events in the device labeling.

Post-approval Requirements and Restrictions: See approval order.