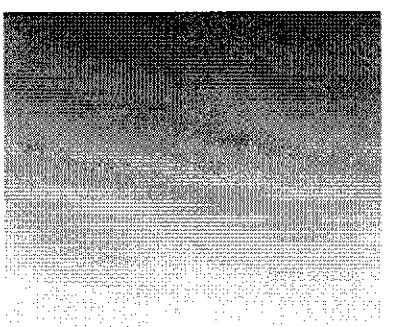
Directions for Use

BIOCELL® Textured and Smooth

SALINE-FILLED BREAST IMPLANTS



INAMED AESTHETICS

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

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Table of Contents

DEVICE DESCRIPTION

INAMED's Saline-Filled Breast Implants are constructed from Room Temperature Vulcanized (RTV) silicone elastomer, made of polydimethylsiloxane. The device is inflated to the desired size with sterile isotonic saline before implantation. Each implant is supplied sterile with a disposable fill tube and reflux valve.

- **Round Breast Implants:**

  Style 68LP: Smooth shell surface, anterior diaphragm valve, low profile.

  Style 68: Smooth shell surface, anterior diaphragm valve, moderate profile.

  Style 68HP: Smooth shell surface, anterior diaphragm valve, high profile.

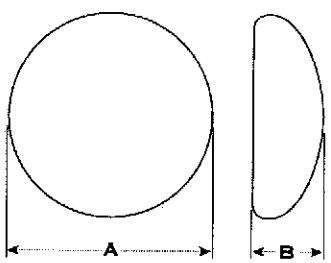
  Style 168: BIOCELL® Textured shell surface, anterior diaphragm valve, moderate projection.

- **Shaped Breast Implants:**

  Style 163: BIOCELL® Textured shell surface, posterior diaphragm valve, full height, full projection.

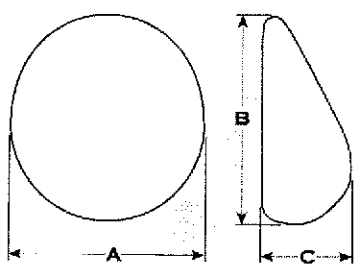
  Style 363LF: BIOCELL® Textured shell surface, anterior diaphragm valve, moderate height, full projection. Style 363 has a ptotic shape to match an existing breast in unilateral reconstruction.

  Style 468: BIOCELL® Textured shell surface, anterior diaphragm valve, full height, moderate projection.



A = Width; B = Projection

ROUND



A = Width; B = Height; C = Projection

SHAPED

6

INDICATIONS

Breast implants are indicated for females for the following indications:

- **Breast Augmentation.** A woman must be at least 18 years old for breast augmentation.
- **Breast Reconstruction.**

CONTRAINDICATIONS

Patient Groups in which the product is contraindicated:

- **Infection.** Active infection anywhere in the body.
- **Breast Cancer.** Existing malignant or pre-malignant cancer of the breast without adequate treatment.
- Augmentation in women who are currently pregnant or nursing.

Surgical Practices in which product use is contraindicated due to compromise of product integrity:

- **Adulterated Fill.** Do not place drugs or substances inside the implant other than sterile saline for injection.
- **Alteration.** Do not alter the implant or valve.
- **Do not inject** through the implant shell.
- **Stacking** of implants: Do not place more than one implant per breast.
- Do not allow the implant to come into contact with povidone iodine.

7

WARNINGS

1. Closed Capsulotomy

DO NOT treat capsular contracture by forceful external compression, which will likely result in implant damage, deflation, folds, and/or hematoma. Capsule firmness must not be treated by overexpansion of the device.

2. Reuse

Breast implants are intended for single use only. Do not resterilize.

3. Avoiding Damage during Surgery

- Care should be taken not to damage the prosthesis with surgical instruments.
- Do not insert or attempt to repair a damaged prosthesis.
- Use care in subsequent procedures such as open capsolotomy, breast pocket revision, hematoma/ seroma aspiration, and biopsy/lumpectomy to avoid damage to the implant shell or valve.
- Do not contact the implant with disposable, capacitor-type cautery devices.

4. Proper Filling

Follow the recommendation on the product data sheet for fill volume; do not overfill or underfill the implant. Following recommended fill volumes can decrease the possibility of shell wrinkling and crease fold failure.

5. Microwave Diathermy

The use of microwave diathermy in patients with breast implants is not recommended, as it has been reported to cause tissue necrosis, skin erosion, and extrusion of the implant.

6. Do not use endoscopic instruments or the periumbilical approach for placement of the implant as damage to the device may occur.

PRECAUTIONS

1. Specific Populations

Safety and Effectiveness has not been established in patients with:

- Autoimmune diseases such as lupus and scleroderma
- A compromised immune system (e.g., currently receiving immunosuppressive therapy)
- Patients with conditions or medications which interfere with wound healing ability (such as poorly controlled diabetes) or blood clotting (such as concurrent Coumadin® therapy).
- Reduced blood supply to breast tissue

2. Mammography

Breast implants may complicate the interpretation of mammographic images by obscuring underlying breast tissue and/or by compressing overlying tissue. Accredited mammography centers and use of displacement techniques are needed to adequately visualize breast tissue in the implanted breast. Presurgical mammography with a follow-up mammogram 6 months to 1 year following surgery may be performed to establish a baseline for future routine mammography.

3. Radiation to the Breast

INAMED has not tested the in vivo effects of radiation therapy in patients who have breast implants. The literature suggests that radiation therapy may increase the likelihood of capsular contracture, necrosis, and extrusion.

4. Long Term Effects

The long term safety and effectiveness of INAMED's breast implants have not been established. INAMED is monitoring the long term (i.e., 10 year) risk of implant rupture, reoperation, implant removal, and capsular contracture.

5. Instructions to Patients:

- *Reoperation* – Patients should be advised that additional surgery to their breast and/or implant will be likely over the course of their life.

- ***Explantation*** – Patients should be advised that implants are not considered life time devices and they will likely undergo implant removal, with or without replacement, over the course of their life. Patients should also be advised that the changes to their breast following explantation are irreversible.
- ***Mammography*** - Patients should be instructed to inform their mammographers about the presence of their implants.
- ***Lactation*** – Patients should be advised that breast implants may interfere with the ability to successfully breast feed.
- ***Breast Examination Techniques*** – Patients should be instructed to perform breast self-examinations monthly and be shown how to distinguish the implant from their breast tissue. The patient should be instructed not to manipulate (i.e., squeeze) the valve excessively, which may cause valve leakage.

Adverse Events

INAMED's Saline-Filled Breast Implants were evaluated in four major open label, multicenter clinical studies: the 1990 Augmentation/Reconstruction Study (AR90), the Large Simple Trial (LST, which involved 2875 patients), the 1995 Augmentation Study (A95, which involved 901 patients), and the 1995 Reconstruction Study (R95, which involved 237 patients). Because the AR90 Study utilized devices and surgical practices that are not current, these data are not reported below. The cumulative Kaplan-Meier risk of first occurrence of adverse events (and 95% confidence interval) reported in greater than 1% of patients is shown in Tables 1 and 2 based on indication.

Table 1
LST: 1-Year Cumulative First Occurrence Kaplan-Meier Adverse Event Risk Rates (95% Confidence Interval), By Patient

Complication	Augmentation		Reconstruction		Revision	
	Rate (%)	(95% CI)	Rate (%)	(95% CI)	Rate (%)	(95% CI)
Capsular Contracture III/IV	7.2	(5.8, 8.6)	12.5	(7.3, 17.8)	11.8	(7.1, 16.4)
Implant Removal with or without Replacement	6.1	(4.9, 7.3)	13.7	(8.7, 18.6)	7.8	(4.2, 11.5)
Leakage/Deflation	3.6	(2.6, 4.5)	2.6	(0.0, 5.2)	5.4	(2.0, 8.8)
Infection	1.5	(0.9, 2.1)	6.2	(2.9, 9.5)	3.3	(1.1, 5.6)

Table 2
A95/R95: 3-Year** and 5-Year Cumulative First Occurrence Kaplan-Meier Adverse Event Risk Rates (95% Confidence Interval), By Patient

Complication	Augmentation (N = 901)				Reconstruction (N = 237)			
	3-Year		5-Year		3-Year		5-Year	
	Rate (%)	(95% CI)	Rate (%)	(95% CI)	Rate (%)	(95% CI)	Rate (%)	(95% CI)
Reoperation	21.1	(18.4, 23.8)	25.9	(23.0, 28.9)	38.7	(32.3, 45.0)	44.5	(37.9, 51.0)
Breast Pain*	15.6	(13.2, 17.9)	17.0	(14.5, 19.5)	15.3	(10.3, 20.2)	17.7	(12.4, 23.0)
Wrinkling*	10.5	(8.4, 12.6)	13.7	(11.3, 16.1)	23.3	(17.5, 29.1)	24.6	(18.6, 30.6)
Asymmetry*	10.1	(8.1, 12.1)	12.2	(10.0, 14.4)	33.0	(26.6, 39.4)	39.0	(32.1, 45.8)
Nipple Paresthesia*	9.3	(7.4, 11.2)	9.8	(7.8, 11.8)	<1	<1	<1	(0.0, 1.2)
Implant Palpability/Visibility*	9.2	(7.2, 11.1)	12.1	(9.8, 14.3)	20.0	(14.5, 25.5)	27.1	(20.6, 33.5)
Capsular Contracture III/IV or grade unknown	8.7	(6.8, 10.6)	11.4	(9.2, 13.5)	25.3	(19.5, 31.2)	35.7	(29.0, 42.4)
Loss of Nipple Sensation*	8.4	(6.5, 10.2)	9.9	(7.8, 11.9)	12.0	(7.4, 16.6)	18.1	(12.5, 23.8)
Implant Malposition*	8.2	(6.3, 10.0)	9.2	(7.3, 11.2)	12.2	(7.8, 16.6)	16.9	(11.7, 22.2)
Implant Removal for Any Reason	7.6	(5.8, 9.4)	11.8	(9.6, 14.0)	22.5	(17.1, 28.0)	28.0	(22.1, 34.0)
Skin Paresthesia*	7.2	(5.5, 9.0)	7.6	(5.9, 9.4)	5.6	(2.5, 8.6)	6.3	(2.9, 9.6)
Scarring Complications	6.4	(4.8, 8.0)	6.5	(4.9 8.2)	6.0	(2.7, 9.2)	6.0	(2.7, 9.2)
Leakage/Deflation	5.0	(3.5, 6.4)	6.8	(5.0, 8.5)	6.2	(2.9, 9.5)	7.5	(3.8, 11.2)
Irritation/Inflammation*	2.9	(1.8, 4.0)	3.2	(2.0, 4.3)	6.6	(3.3, 9.8)	6.6	(3.3, 9.8)
Seroma	2.6	(1.6, 3.7)	2.6	(1.6, 3.7)	3.9	(1.4, 6.4)	3.9	(1.4, 6.4)
Hematoma	1.6	(0.7, 2.4)	1.7	(0.8, 2.5)	1.3	(0.0, 2.8)	1.3	(0.0, 2.8)
Skin Rash	1.6	(0.8, 2.4)	1.9	(1.0, 2.8)	3.3	(0.9, 5.7)	3.3	(0.9, 5.7)
Capsular Calcification*	1.2	(0.4, 1.9)	1.8	(0.9, 2.7)	4.7	(1.9, 7.6)	5.4	(2.3, 8.6)
Infection	<1	<1	1.0	(0.3, 1.6)	4.8	(2.0, 7.5)	6.0	(2.8, 9.2)
Delayed Wound Healing*	<1	<1	<1	<1	2.7	(0.6, 4.9)	2.7	(0.6, 4.9)
Implant Extrusion	<1	<1	<1	<1	2.6	(0.6, 4.7)	3.2	(0.9, 5.6)
Tissue/Skin Necrosis	<1	<1	<1	<1	3.6	(1.1, 6.0)	3.6	(1.1, 6.0)

* These complications were assessed with severity ratings. Only the rates for moderate, severe, or very severe (excludes mild and very mild ratings) are shown.

** 3-year risk rates as reported in original PMA submission.

Of the 901 patients in the A95 Study, at least one additional surgical procedure was performed on 204 patients (23%) through 4 years and 224 patients (25%) through 5 years. A total of 402 surgical procedures were performed through 4 years and 463 procedures were performed through 5 years in the A95 Study.

Of the 237 patients in the R95 Study, at least one additional surgical procedure was performed on 171 patients (72%) through 4 years, involving 433 surgical procedures. Most of the 433 procedures were planned nipple reconstruction and nipple/areolar tattoo procedures. In terms of unplanned procedures, a total of 151 procedures were performed through 4 years and 159 procedures were performed through 5 years in the R95 Study.

Table 3 shows the types of additional surgical procedures performed through 4 and 5 years in the A95/R95 Studies based on the total number of additional surgical procedures.

Table 3
A95/R95: Types of Additional Surgical Procedures through 4 Years* and 5 Years

Type of Additional Surgical Procedures	Augmentation*				Reconstruction*			
	Through 4 Years N = 402		Through 5 Years N = 463		Through 4 Years N = 151		Through 5 Years N = 159	
	n	percent	n	percent	n	percent	n	percent
Implant Removal w/Replacement**	122	30	156	34	45	30	49	31
Capsule Related**	78	19	86	19	18	12	13	8
Add/Remove Saline	46	11	49	11	9	6	10	6
Scar Revision/Wound Repair	36	9	42	9	29	19	30	19
Mastopexy	28	7	28	6	0	0	0	0
Aspiration	28	7	29	6	7	5	7	4
Reposition Implant	19	5	20	4	6	4	7	4
Biopsy/Lump Removal	16	4	21	5	7	5	7	4
Implant Removal without Replacement	10	3	10	2	17	11	21	13
Exploration of Breast Area or Implants	8	2	6	1	0	0	0	0
Removal of Skin Lesion or Cyst	6	2	10	2	1	1	3	2
Skin Related Procedure	4	1	3	1	6	4	6	4
Unplanned Nipple-Related Procedure	1	<1	1	<1	3	2	3	2
Other Procedures****	0	0	0	0	3	2	3	2

*As reported in original PMA submission with additional data clarification.
**Capsule related includes capsulectomy, capsulotomy, and capsulorraphy.
*** Some removals were replaced with an Inamed implant, while others were replaced with a non-Inamed implant.
**** Other procedures through 5 years include liposuction, and placement of a stacked implant.

Of the 901 patients in the A95 Study, at least one reoperation was performed on 204 patients (23%) through 4 years, and 225 patients (25%) through 5 years. A total of 257 reoperations were performed through 4 years, and 293 through 5 years in the A95 Study. The primary reason for reoperation through 5 years was implant deflation at 18.1%.

Of the 237 patients in the R95 Study, at least one reoperation was performed on 94 patients (40%) through 4 years, and 99 patients (42%) through 5 years. A total of 117 reoperations were performed through 4 years, and 125 through 5 years in the R95 Study. The primary reason for reoperation through 5 years was capsular contracture at 27.2%.

Table 4 shows the reasons for reoperation through 4 and 5 years in the A95/R95 Studies based on the total number of reoperations.

Table 4
A95/R95: Reasons for Reoperation Through 4 Years and 5 Years

Reasons for Reoperation	Augmentation				Reconstruction			
	Through 4 Years N = 257		Through 5 Years N = 293		Through 4 Years N = 117		Through 5 Years N = 125	
	n	percent	n	percent	n	percent	n	percent
Capsular Contracture	47	18.3	52	17.7	31	26.5	34	27.2
Leakage/Deflation	45	17.5	53	18.1	9	7.7	11	8.8
Patient Choice	38	14.8	45	15.3	13	11.1	13	10.4
Hematoma/Seroma	25	9.7	26	8.9	6	5.1	6	4.8
Implant Malposition	24	9.3	28	9.6	12	10.3	11	8.8
Lump/Mass/Cyst	20	7.8	25	8.5	9	7.7	10	8.0
Scarring	18	7.0	21	7.2	10	8.5	10	8.0
Ptosis	14	5.4	17	5.8	0	0.0	0	0.0
Asymmetry	13	5.1	14	4.8	25	21.4	25	20.0
Add/Remove Saline	12	4.7	14	4.7	4	3.5	4	3.2
Wrinkling	8	1.9	8	2.7	3	2.6	5	4.0
Unsatisfactory Nipple Result	4	1.6	5	1.7	1	0.9	1	0.8
Delayed Wound Healing	4	1.6	4	1.4	2	1.7	2	1.6
Skin Lesion/Cyst	3	1.2	3	1.0	1	0.9	2	1.6
Infection	3	1.2	4	1.4	8	6.8	9	7.2
Implant Palpability	2	0.8	4	1.4	2	1.7	3	2.4
Breast Pain	2	0.8	2	0.7	6	5.1	9	4.8
Irritation	1	0.4	1	0.3	0	0.0	0	0.0
Implant Extrusion	1	0.4	1	0.3	5	4.3	5	4.0
Tissue/Skin Necrosis	0	0.0	0	0.0	6	5.1	6	4.8
Suture/Incision Observation	0	0.0	0	0.0	0	0.0	0	0.0
Capsule Calification	0	0.0	1	0.3	0	0.0	0	0.0
Total	**281**	**109.3***	**328**	**111.9***	**153**	**130.8***	**163**	**130.4***

*Total is greater than 100% because some reoperations were performed for multiple reasons.

Of the 901 augmentation patients in A95, there were 81 patients (9.0%) who had 132 implants removed through 4 years. A total of 98 patients had 166 implants removed through 5 years. Of the 237 reconstruction patients in R95, there were 58 patients (24.5%) who had 62 implants through 4 years. A total of 62 patients had 70 implants removed through 5 years. Of the 166 augmentation implants removed through 5 years, 94% were replaced; of the 70 reconstruction implants removed through 5 years, 70% were replaced. The primary reason for implant removal is shown in Table 5 below based on the number of implants removed.

Table 5
A95/R95: Reasons for Implant Removal Through 4 Years* and 5 Years

Primary Reason for Implant Removal	Augmentation				Reconstruction			
	Through 4 Years N = 132		Through 5 Years N = 166		Through 4 Years N = 62		Through 5 Years N = 70	
	n	percent	n	percent	n	percent	n	percent
Patient Choice	57	43	72	43	14	23	15	21
Leakage/Deflation**	44	33	54	33	10	16	12	17
Capsular Contracture	13	10	17	10	16	26	22	31
Wrinkling	6	5	6	1	2	3	2	3
Asymetry	4	3	3	2	2	3	1	1
Breast Pain	3	2	3	2	0	0	0	0
Malposition	2	2	2	1	4	6	3	4
Iatrogenic Injury	1	1	1	1	0	0	0	0
Infection	1	1	1	1	6	10	7	10
Implant Extrusion	1	1	1	1	4	6	4	6
Implant Palpability/Visibility	0	0	6	4	0	0	0	0
Recurrent Breast Cancer	0	0	0	0	2	3	1	1
Other***	0	0	0	0	2	3	3	4
Total	**132**	**100**	**166**	**100**	**62**	**100**	**70**	**100**

* As reported in original PMS submission with some data recategorization of "Other".

** Includes unreported unknown (n=1 augmentation through 5 years, n=1 reconstruction through 4 years, n=2 reconstruction through 5 years).

*** Reconstruction: Through 4 years, other reasons were: abnormality of CT scan at mastectomy site (n=1), poor tissue expansion due to radiation (n=1). Through 5 years, other reasons were: abnormality of CT scan at mastectomy site (n=1), poor tissue expansion due to radiation (n=1), second stage breast reconstruction (n=1).

17

Potential Adverse Events

The following is a list of potential adverse events that may occur with breast implant surgery. Some of these adverse events have been reported in tables 1 and 2 above. The risks include: implant deflation/ leakage, additional surgery, capsular contracture, infection, Toxic Shock Syndrome, necrosis, hematoma, seroma, extrusion, breast pain, changes in nipple sensation, changes in breast sensation, dissatisfaction with cosmetic results (wrinkling, folding, displacement, asymmetry, palpability, visibility, ptosis, sloshing), calcific deposits, irritation/inflammation, delayed wound healing, hypertrophic scarring, breast tissue atrophy/chest wall deformity, difficulty/inability in breast feeding, and inability to adequately visualize breast lesions with mammography. In addition to these potential adverse events, there have been concerns with certain systemic diseases.

- **Connective Tissue Disease**
  Concern over the association of breast implants to the development of autoimmune or connective tissue diseases, such as lupus, scleroderma, or rheumatoid arthritis, was raised because of cases reported in the literature with small numbers of women with implants. A review of several large epidemiological studies of women with and without implants indicates that these diseases are no more common in women with implants than those in women without implants.

- **Cancer**
  Published studies indicate that breast cancer is no more common in women with implants than those without implants.

- **Second Generation Effects**
  There have been concerns raised regarding potential damaging effects on children born of mothers with implants. A review of the published literature on this issue suggests that the information is insufficient to draw definitive conclusions.

CLINICAL STUDIES OVERVIEW

1. Study Design

The safety and effectiveness of INAMED's Saline-Filled Breast Implants were evaluated in four open label, multicenter clinical studies: the 1990 Augmentation/Reconstruction Study (AR90), the Large Simple Trial (LST), the 1995 Augmentation Study (A95), and the 1995 Reconstruction Study (R95). Patients studied were those seeking implant surgery for augmentation or reconstruction of the breast. Because the 1990 Study utilized devices and surgical practices which are not current, these data are not reported below. The LST Study was designed as a one year study to assess the four safety outcomes of capsular contracture, infection, implant leakage/deflation, and implant removal for a large number of patients.

The A95/R95 Studies were designed as 5 year studies to assess safety and effectiveness. Patient follow-up was yearly for 5 years. Safety assessments in the A95/R95 Studies consisted of adverse event rates and rates of secondary surgical treatment. Effectiveness assessments in the A95/R95 Studies consisted of patient satisfaction, breast size change, and measures of body esteem/self esteem/body image. A95/R95 data through 3 years (with partial 4 year data) was presented to FDA for PMA approval. After PMA approval, INAMED transitioned data collection to a post-approval study. The first phase of this post-approval study consisted of completion of the A95 and R95 Studies, with collection of all risk/benefit information through 5 years post-implant. The second phase of the post-approval study consists of a patient survey-based study, with collection of specific risk/benefit information through 6-10 years post implant.

The data presented to FDA for PMA approval (i.e., 4-year data) along with post-approval data through 5 years and 7 years are included in this brochure. Please note that the data/tables labeled "through 4 years" are only partial 4-year study data as reported in the original PMA or current FDA-approved labeling.

2. Patient Accounting and Baseline Demographic Profile

The LST Study enrolled 2,333 augmentation patients, 225 reconstruction patients, and 317 revision patients with an overall 1-year follow-up compliance rate of 62%. The A95 Study enrolled 901 augmentation patients, with 77% returning for their 3-year follow-up visit. Of those A95 patients available to be seen for their 5-year follow-up visit, 81% returned and were seen at 5 years after implant surgery. The R95 Study enrolled 237 reconstruction patients, with 71% returning for their 3-year follow-up visit. Of those R95 patients available to be seen for their 5-year follow-up visit, 80% returned and were seen at 5 years after implant surgery. Demographic

information obtained from the 1995 Studies revealed that nearly 90% of both augmentation and reconstruction patients were Caucasian and more than half of study participants were married. The median age of the augmentation patients was 32 years (range: 19-66); for reconstruction patients the median age was 47 years (range: 25-77). With respect to surgical baseline factors in the 1995 Studies, for augmentation patients, the most frequently used devices were textured round, the most common incision sites were periareolar and inframammary, and the most frequent placement of the implant was submuscular. For reconstruction patients, the most frequently used devices were textured BioDIMENSIONAL®, the most common incision site was the mastectomy scar, and the most frequent placement of the implant was submuscular.

3. Safety Outcomes

The LST safety outcomes are presented in Table 1 above. The A95 Study and R95 Study safety outcomes for primary implantation are presented in Tables 2–4 above. As additional safety information, Tables 5a and 5b below show the 2-year and 3-year cumulative Kaplan-Meier adverse event risk rates of first occurrence following implant replacement (i.e., revision) on a by implant basis for the A95 and R95 Studies. There were 126 augmentation implants and 40 reconstruction implants in the A95/R95 Studies that were removed and replaced with INAMED study devices.

Table 5a

A95: 2-Year* and 3-Year Cumulative First Occurrence Kaplan-Meier Adverse Event Risk Rates (95% Confidence Interval) Following Augmentation Implant Replacement, by Implant

Complication Following Replacement of Augmentation Implants	2-Year Risk Rate* N = 108 Implants		3-Year Risk Rate N = 126 Implants	
	%	95% CI	%	95% CI
Removal/Replacement	5.4	(0.2, 10.5)	18.3	(9.4, 27.1)
Leakage/Deflation	9.1	(3.4, 14.7)	9.3	(3.1, 15.6)
Capsule Contracture III/IV	7.3	(1.5, 13.0)	7.6	(2.5, 12.7)
Infection	1.0	(0.0, 3.0)	2.5	(0.0, 5.3)

* As reported in original PMA submission with additional data clarification.

Table 5b
R95: 2-Year* and 3-Year Cumulative First Occurrence Kaplan-Meier Adverse Event Risk Rates (95% Confidence Interval) Following Reconstruction Implant Replacement, by Implant

Complication Following Replacement of Reconstruction Implants	2-Year Risk* Rate N = 40 Implants		3-Year Risk Rate N = 40 Implants	
	%	95% CI	%	95% CI
Capsule Contracture III/IV	32.6	(16.6, 48.5)	33.8	(18.0, 49.5)
Removal/Replacement	25.5	(9.8, 41.3)	26.9	(12.5, 41.2)
Leakage/Deflation	5.3	(0.0, 12.5)	9.5	(0.0, 20.1)
Infection	7.3	(0.0, 17.3)	2.9	(0.0, 8.4)

* As reported in original PMA submission with correction of capsular contracture rate.

CTD and Breast Disease

Tables 6a and 6b summarize post-implant observations from the A95 and R95 Studies pertaining to connective tissue/autoimmune (CTD) disease and breast disease (including breast carcinoma). These data should be interpreted with caution in that there was no comparison group of similar women without implants. Unconfirmed reports were based on self-reports by the patients. Confirmed reports were based on a diagnosis by a physician. Data pertaining to effects on offspring and mammographic detection of tumors/lesions were not collected in these studies. From 4 to 5 years, the total number of confirmed CTD and breast disease reports has changed due to the identification of new reports, the removal of unconfirmed reports found to be false, and/or the recategorization of reports between the 4th and 5th year. With regard to CTD, from 4 to 5 years, there have been 11 new reports (2 confirmed, 9 unconfirmed) among the augmentation patients and 4 new reports (all unconfirmed) among the reconstruction patients. With regard to breast disease, from 4 to 5 years, there have been 7 new reports among the augmentation patients and 7 new reports among the reconstruction patients.

Table 6a
A95/R95: Reports of CTD Through 4 Years* and 5 Years, By Patient

Rheumatic Disease	Augmentation				Reconstruction			
	Through 4 Years		Through 5 Years		Through 4 Years		Through 5 Years	
	No. of Confirmed Reports	No. of Unconfirmed Reports	No. of Confirmed Reports	No. of Unconfirmed Reports	No. of Confirmed Reports	No. of Unconfirmed Reports	No. of Confirmed Reports	No. of Unconfirmed Reports
Graves' Disease	2	0	3	0	1	0	1	0
Hyperthyroiditis	1	2**	2	1	0	0	0	0
Inflammatory Bowel Disease	0	0	0	1	0	1	0	0
Lupus Erythematosus and/or Rheumatoid Arthritis	0	3	0	1	0	1	0	3
Thyroiditis	0	2	0	4	0	2	0	1
Chronic Fatigue Syndrome or Fibromyalgia	2	0	2	4	0	0	0	0
Seronegative Spondylarthritis	0	0	0	1	0	0	0	0
Raynaud's Phenomenon, Graves' Disease, Hyperthyroiditis, and Rheumatoid Arthritis	0	0	0	1**	0	0	0	0
Total	**5**	**7**	**7**	**13**	1	**4**	**1**	**4**

*As reported in original PMA submission.

**Patient was recategorized at 5-year timepoint.

Table 6b
A95/R95: Reports of Breast Disease 4 Years* and 5 Years, By Patient

Breast Disease Observation	Augmentation		Reconstruction	
	Through 4 Years n	Through 5 Years n	Through 4 Years n	Through 5 Years n
Benign	66	80	72	75
Malignant	1	1	19	24
Unknown Outcome	7	0	1	0

* As reported in original PMA submission with additional data clarification:
Benign includes 22 additional augmentation reports and 61 additional reconstruction reports,
and unknown outcome includes 2 fewer augmentation reports.

4. Effectiveness Outcomes

Effectiveness of saline-filled breast implants was assessed by a variety of outcomes, including bra cup size change (augmentation patients only), patient satisfaction, body image, body esteem, and self concept. These outcomes were assessed for patients with both original and replacement saline devices before implantation and at 3 years after surgery, except for bra size and satisfaction. Bra size was measured within the first year and a half after surgery. Satisfaction was measured at every follow-up visit through 5 years.

Augmentation
859 of the original 901 augmentation patients (95%) at 18 months were included in an analysis of cup size (5% did not provide data because pre/post measurements were not obtained or replacement/ removal occurred prior to obtaining a post measurement). Of these 859 patients, the following shows the percentage of patients experiencing various changes in cup size:

- Increase by 1 cup size: 38%
- Increase by 2 cup sizes: 49%
- Increase by 3 cup sizes: 9%
- No Increase: 4%

683 of the original 901 augmentation patients (76%) were included in an analysis of satisfaction at 5 years (24% were not included because satisfaction data was not obtained or implant replacement/ removal occurred prior to 5 years). Of these 683 patients, 95% indicated being satisfied with their breast implants at 5 years. Before implantation, augmentation patients scored higher (better) than the general U.S. female population on the SF-36 and MOS-20 scales, which measure general health-related quality of life. After 3 years, augmentation patients showed a worsening in their SF-36 and MOS-20 scores. The following two scales showed no change over the 3 years: The Tennessee Self Concept Scale (which measures overall self concept) and The Body Esteem Scale (which measures overall self esteem related specifically to one's body). The Rosenberg Self Esteem Scale (which measures overall self esteem) showed a slight improvement over the 3 years. The Semantic Differential Scale (which measures attitudes about your breasts compared to attitudes about yourself) showed that patients experienced an increased positive attitude towards their breasts compared to themselves over the 3 years.

Reconstruction

137 of the original 237 reconstruction patients (58%) were included in an analysis of satisfaction at 5years (42% were not included because satisfaction data was not obtained or implant replacement/ removal occurred prior to 5 years). Of these 137 patients, 89% indicated being satisfied with their breast implants at 5 years. Before implantation, reconstruction patients scored higher (better) than the general U.S. female population before implantation on some SF-36 scales, which measure general health-related quality of life. After 3 years, reconstruction patients showed an improvement in some of their SF-36 and MOS- 20 scores. The following three scales showed no change over the 3 years: The Tennessee Self Concept Scale (which measures overall self concept), The Rosenberg Self Esteem Scale (which measures overall self esteem), and The Body Esteem Scale (which measures overall self esteem related specifically to one's body). The Semantic Differential Scale (which measures attitudes about your breasts compared to attitudes about yourself) showed that patients experienced an increased positive attitude towards their breasts compared to themselves over the 3 years.

Post-Approval Study

The post-approval study transitioned patients from data collection via physicians (0-5 years post-implantation) to data collection via mailed patient-completed surveys (6-10 years post-implantation). The tables below present data collected through 7 years post-implantation. 85% of the augmentation patients and 83% of the reconstruction patients expected for follow-up at 7 years returned surveys to INAMED according to study protocol. The surveys at 7-years showed 88% of the augmentation patients and 88% of the reconstruction patients who provided satisfaction scores indicated being satisfied with their breast implants at 7 years post-implant. The cumulative Kaplan-Meier risk of first occurrence of adverse events (and 95% C.I.) are shown in Table 7 below.

Table 7
Post Approval: 7 Year First Occurrence Kaplan-Meier Adverse Event Risk Rates (95% Confidence Interval), By Patient

Complication	7-Year Risk			
	Augmentation (N = 901)		Reconstruction (N = 237)	
	Rate (%)	(95% CI)	Rate (%)	(95% CI)
Reoperation	29.9	(26.8, 32.9)	48.0	(41.4, 54.7)
Breast Pain	24.5	(21.5, 27.4)	25.9	(19.5, 32.3)
Capsular Contracture	15.7	(13.2, 18.2)	42.6	(35.6, 49.6)
Implant Removal	14.5	(12.2, 16.9)	31.3	(24.1, 37.5)
Implant Deflation	9.8	(7.8, 11.9)	12.4	(7.6, 17.2)

Of the 901 augmentation patients in the PASS Study, at least one reoperation was performed on 261 patients (29%) through 7 years. A total of 343 reoperations were performed. The primary reason for reoperation through 7 years on augmentation patients was implant deflation at 19.2%.

Of the 237 reconstruction patients in the PASS Study, at least one unplanned reoperation was performed on 107 patients (45.1%) through 7 years. A total of 138 unplanned reoperations were performed. The primary reason for reoperation through 7 years on reconstruction patients was capsular contracture at 25.4%.

Table 8 shows the reasons for reoperation through 7 years in the PASS Study based on the total number of reoperations.

Table 8
Post Approval: Reasons for Reoperation Through 7 Years

Reasons for Reoperation	7-Year Augmentation (N = 343 Reoperations)		7-Year Reconstruction (N = 138 Reoperations)	
	n	%	n	%
Implant Deflation	66	19.2	16	11.6
Patient Choice	61	17.8	16	11.6
Capsular Contracture	54	15.7	35	25.4
Lump/Mass/Cyst	43	12.5	12	8.7
Implant Malposition	30	8.7	13	9.4
Hemotoma/Seroma	27	7.9	6	4.3
Scarring	22	6.4	11	8.0
Ptosis	21	6.1	1	0.7
Add/Remove Saline	18	5.3	4	2.9
Asymmetry	14	4.1	25	18.1
Wrinkling	8	2.3	5	3.6
Implant Palpability	5	1.5	3	2.2
Unsatisfactory Nipple Result	5	1.5	2	1.4
Delayed Wound Healing	4	1.2	2	1.4
Infection	4	1.2	9	6.5
Skin Lesion/Cyst	3	0.9	2	1.4
Breast Pain	2	0.6	6	4.3
Capsule Calcification	1	0.3	0	0.0
Implant Extrusion	1	0.3	5	3.6
Irritation	1	0.3	0	0.0
Cancer	0	0.0	1	0.7
Tissue/Skin Necrosis	0	0.0	6	4.3
Total	**390**	**113.8**	**180**	**130.1**

* Some reoperations were performed for multiple reasons; all reasons are included in this table.

The main reasons for implant removal through 7 years are shown in Table 9 below. Through 7 years, 213 implants were removed from 124 augmentation patients and 81 implants were removed from 69 reconstruction patients.

Table 9
Post Approval: Reasons for Implant Removal Through 7 Years

Primary Reason for Implant Removal	Augmentation Through 7 Years N = 213		Reconstruction Through 7 Years N = 81	
	n	percent	n	percent
Patient Choice	90	42.3	19	23.5
Implant Deflation	68	31.9	20	24.7
Capsular Contracture	20	9.4	20	24.7
Wrinkling	8	3.8	2	2.5
Implant Malposition	8	3.8	3	3.7
Implant Palpability/Visibility	6	2.8	0	0.0
Asymmetry	6	2.8	2	2.5
Breast Pain	3	1.4	0	0.0
Iatrogenic Injury	1	0.5	0	0.0
Infection	1	0.5	7	8.6
Implant Extrusion	1	0.5	4	4.9
Breast Mass/Lump/Cyst	1	0.5	0	0.0
Hemotoma	0	0.0	0	0.0
Other*	0	0.0	4	4.9
Total	**213**	**100.1**	**81**	**100.0**

* Other reasons as reported by the physician were: Recurrent Carcinoma (n-=1), Abnormality on CT Scan at Mastectomy Site (n=1), Tissue expansion went poorly due to radiation (n=1), Second stage breast Recon (n=1).

INSTRUCTIONS FOR USE

NOTE: Back-up breast implants must be available during the procedure.

DO NOT Stack more than one implant per breast.

Single Use

This product is intended for **single use only**. Do not reuse explanted implants.

Product Identification

Product labels accompany each device within the internal product packaging. The product labels provide product-specific information. Product labels may be attached to the patient's chart for identification purposes. The Device Identification Card should be provided to the patient for personal reference.

Surgical Planning

Proper surgical planning such as allowance for adequate tissue coverage, implant site (i.e., submuscular vs. subglandular), incision site, implant type etc. should be made preoperatively. The surgeon must carefully evaluate implant size and contour, incision placement, pocket dissection, and implant placement criteria, with respect to the patient's anatomy and desired physical outcome. Planning should include clear delineation of aesthetic goals to ensure mutual understanding between surgeon and patient.

Sterile Product

Each sterile saline-filled breast implant is supplied in a sealed, double primary package. Style-specific sterile product accessories are also supplied within the product packaging. Sterility of the implant is maintained only if the thermoform packages, including the package seals, are intact. Use standard procedures to maintain sterility during transfer of the breast implant to the sterile field. Remove the breast implant and accessories from their packages in an aseptic environment and using talc-free gloved hands.

DO NOT use the product if the thermoform packages or seals have been damaged.

DO NOT implant damaged or contaminated breast implants.

DO NOT store the breast implant with the fill tube in place, which may damage the integrity of the valve seal.

DO NOT resterilize the product.

NEVER, under any circumstances, attempt to resterilize using ethylene oxide, which is known to cause adverse tissue reaction if not completely removed from the device. Avoid unnecessary exposure of the breast implant to lint, talc, sponge, towel, skin oils, and other contaminants. Prior to use, keep the breast implant in the inner thermoform and covered to prevent contact with airborne and surgical field particulate contaminants.

1. Peel open the lid of the outer thermoform package.

2. Invert the outer thermoform over the sterile field, allowing the sealed inner thermoform to gently fall into the field.

3. Peel open the lid of the inner package using the pull tab.

4. Gently retrieve the breast implant.

Surgical Procedure

Breast augmentation with saline-filled implants can be carried out through several different incisions including inframammary, periareolar, or transaxillary. The transumbilical incisional approach is not recommended. Some surgeons advocate a "no-touch" technique, which requires significant attention to minimizing contact between the patient's skin and the implant.

Pocket dissection should be planned out preoperatively and be performed accurately and with minimal trauma. Excellent hemostasis is important to avoid postoperative hematoma. The implant may be placed subglandularly or subpectorally depending upon the balance of cosmetic and medical considerations in any given patient. The size and shape of the device may be determined preoperatively by means of dimensional planning or intraoperatively with the help of temporary sizer devices. The implant may be filled with saline either before or after insertion. If inserted without saline, the implant may be inserted as received (i.e., filled with air), or the air may be evacuated prior to insertion. Regardless of which insertion technique is used, it is important to ultimately evacuate as much air from the implant as possible. It is also important to maintain proper orientation of any BioDIMENSIONAL® implant. The incision for the placement of the implant should be securely closed and in several layers, whenever possible. Drains are optional.

Breast Reconstruction is generally carried out in the mastectomy scar. Special care must be used in breast reconstruction to make sure that appropriate amounts of healthy tissue be available to cover the

implant and that the implant be properly sized and positioned based upon careful preoperative planning. Educational materials are available through the Inamed Customer Care Department to supplement surgical knowledge of the dimensional techniques intended for use with BioDIMENSIONAL® styles.

Maintaining Hemostasis/Avoiding Fluid Accumulation

Postoperative hematoma and seroma may be minimized by meticulous attention to hemostasis during surgery, and possibly also by postoperative use of a closed drainage system. Persistent, excessive bleeding must be controlled before implantation. Any postoperative evacuation of hematoma or seroma must be conducted with care to avoid breast implant contamination, or damage from sharp instruments.

Technique for Using Breast Implants with Diaphragm Valve

The fill volume range is specified on the product package labeling and data sheet. Following recommended fill volumes can decrease the possibility of shell wrinkling and crease fold failure.

DO NOT underfill or overfill the breast implant beyond the range specified.

DO NOT use excessive force during any of the steps in the following procedure.

DO NOT damage the breast implant with sharp surgical instruments such as needles and scalpels, or by excessive handling and manipulation during introduction into the surgical pocket.

1. Fill tube insertion

Prepare the fill tube by attaching the reflux valve to the Luer adapter of the fill tube as shown in **Figure 1**. The reflux valve prevents back-flow during intraoperative filling. This two-way valve opens when a syringe is attached, and closes when the syringe is removed.

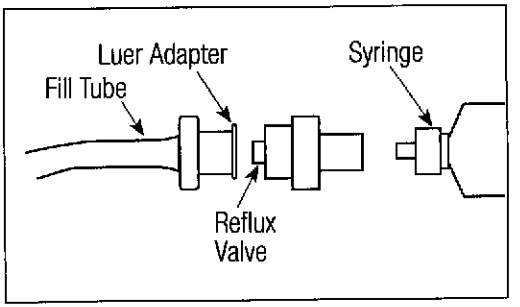


Figure 1

Figure 2 shows a cross section of the diaphragm valve with the strap closure in place and the valve closed. To insert the fill tube, wet the tip of the fill tube in sterile saline for injection and push the strap closure to one side of the valve entrance.

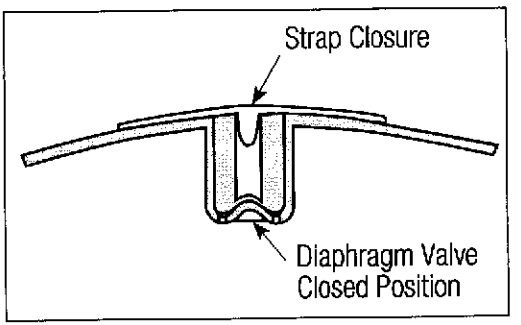


Figure 2

Insert the fill tube by gently pushing the fill tube tip into the valve entrance. Do not use excessive force while inserting the fill tube tip. When the fill tube flange nears or makes contact with the implant shell, the fill tube is in the proper position and the diaphragm valve is open (**Figure 3**).

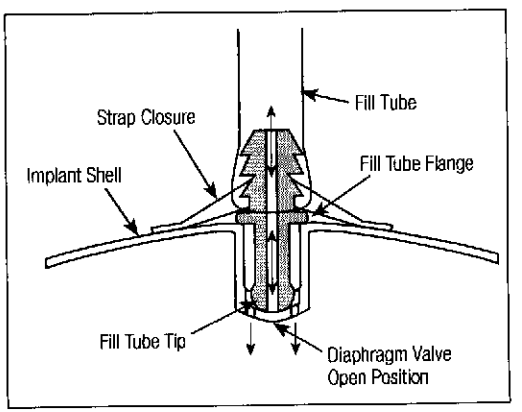


Figure 3

2. *Air aspiration*

After the fill tube is properly inserted, remove any air from the breast implant by aspiration with an empty sterile syringe attached to the reflux valve on the fill tube.

3. *Placement*

To assist with placement, a sterile BIOCELL® Delivery Assistance Sleeve is available separately. Use of this sleeve for insertion of BIOCELL® textured breast implants provides a shell/tissue interface with less friction. Insert the breast implant into one end of the sleeve. Insert the proximal end of the sleeve into the surgically-prepared pocket. With the tissue retracted, the sleeve can be twisted at its distal end to gently guide the breast implant into the pocket. Once the implant is inserted, gently remove the sleeve, and verify the correct orientation of the valve and the implant.

DO NOT use lubricants to facilitate placement, which create the risk of pocket contamination.

Lubricants may also affect tissue adherence.

DO NOT use the breast implant for expansion or dissection of the pocket.

4. *Filling*

Use a syringe filled with sterile, pyrogen-free Sodium Chloride U.S.P. Solution for Injection to fill the prosthesis and fill to a volume within the recommended fill range specified on the product package labeling and data sheet. Only sterile pyrogen-free Sodium Chloride U.S.P. Solution for Injection drawn from its original container should be used. As it is known that bacterial infections may result from contaminated saline, it is recommended that a new sterile saline container be used with each surgery and implant-filling procedure.

NOTE: The order of filling, placement, and orientation may vary with surgeon preference and technique.

5. *Residual Air*

After filling is completed, aspirate any residual air bubbles. Then use gentle traction to remove the fill tube from the valve, taking care to avoid damage to shell or valve.

6. *Diaphragm Valve Closure*

Use gentle traction to remove the fill tube from the valve, taking care to avoid damage to shell or valve. Verify that the diaphragm valve is clear of particulates. Once the fill tube tip is removed the diaphragm valve is closed. To help retard tissue ingrowth or fluid accumulation in the valve entrance, engage the strap closure as follows: using the thumb and forefinger, compress the valve seat and the strap to snap the valve plug into place as shown in **Figure 2.**

Information a Physician Should Provide to the Patient

Breast implantation is an elective procedure and the patient must be well counseled on the risk-benefit relationship. The surgeon should provide each prospective patient with the following:

- Making an Informed Decision

  This brochure can be used to facilitate patient education in the risks and benefits of saline-filled breast implant surgery. The patient should be advised to wait a week after reviewing and considering this information before deciding whether to have augmentation surgery.

- Device Identification Card

  Enclosed with each saline-filled breast implant is a Device Identification Card. To complete the Device Identification Card, place one device identification sticker for each implant on the back of the card. Stickers are located on the internal product packaging attached to the label. If a sticker is unavailable, the lot number, catalog number and description of the device may be copied by hand from the device label. Patients should be provided with these cards for personal reference.

Specific Product Information

BIOCELL® Delivery Assistance Sleeve

Sterile BIOCELL® Delivery Assistance Sleeves are available from your INAMED Aesthetics Sales Representative or Customer Care Department at 800.766.0171.

Returned Goods Policy

Product returns should be handled through a INAMED Aesthetics Sales Representative or through the Customer Care Department at 800.766.0171. Return value is based on time limitations. All package seals must be intact to be eligible for return. Returned products may be subject to a restocking charge. Certain products are non-returnable, including Zyderm® and Zyplast®.

Reporting and Return of Explanted Devices

The reason for explantation should be reported and the explanted device returned to INAMED Corporation. In the event of such an explantation, please contact Product Support at 800.624.4261 for an Explant Kit and explant return instructions.

ConfidencePlus™ Limited Warranties

The ConfidencePlus™ Limited Warranties provide lifetime replacement and limited financial reimbursement in the event of loss of shell integrity resulting in implant deflation, subject to certain conditions as fully discussed in the ConfidencePlus™ literature. For more information, please contact Product Support at 800.624.4261.

Product Ordering

To order directly in the U.S.A or for product information, please contact your local INAMED Aesthetics Sales Representative or the INAMED Customer Care Department at 800.766.0171.

INAMED
AESTHETICS

www.InamedAesthetics.com

5540 Ekwill Street
Santa Barbara, CA 93111
800.624.4261

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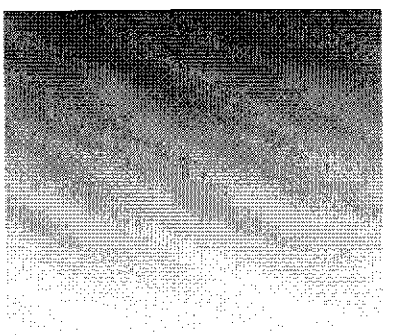
Directions for Use

BIOCELL® Textured and Smooth

SALINE-FILLED BREAST IMPLANTS



INAMED AESTHETICS

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

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

Table of Contents

DEVICE DESCRIPTION

INAMED's Saline-Filled Breast Implants are constructed from Room Temperature Vulcanized (RTV) silicone elastomer, made of polydimethylsiloxane. The device is inflated to the desired size with sterile isotonic saline before implantation. Each implant is supplied sterile with a disposable fill tube and reflux valve.

- **Round Breast Implants:**

  Style 68LP: Smooth shell surface, anterior diaphragm valve, low profile.

  Style 68: Smooth shell surface, anterior diaphragm valve, moderate profile.

  Style 68HP: Smooth shell surface, anterior diaphragm valve, high profile.

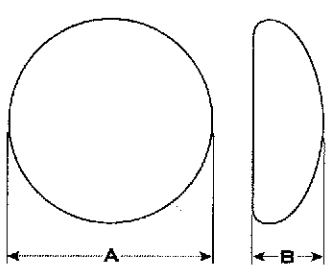
  Style 168: BIOCELL® Textured shell surface, anterior diaphragm valve, moderate projection.

- **Shaped Breast Implants:**

  Style 163: BIOCELL® Textured shell surface, posterior diaphragm valve, full height, full projection.

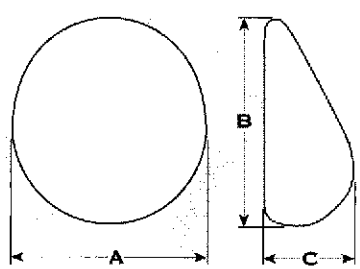
  Style 363LF: BIOCELL® Textured shell surface, anterior diaphragm valve, moderate height, full projection. Style 363 has a ptotic shape to match an existing breast in unilateral reconstruction.

  Style 468: BIOCELL® Textured shell surface, anterior diaphragm valve, full height, moderate projection.



A = Width; B = Projection

ROUND



A = Width; B = Height; C = Projection

SHAPED

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INDICATIONS

Breast implants are indicated for females for the following indications:

- **Breast Augmentation.** A woman must be at least 18 years old for breast augmentation.
- **Breast Reconstruction.**

CONTRAINDICATIONS

Patient Groups in which the product is contraindicated:

- **Infection.** Active infection anywhere in the body.
- **Breast Cancer.** Existing malignant or pre-malignant cancer of the breast without adequate treatment.
- Augmentation in women who are currently pregnant or nursing.

Surgical Practices in which product use is contraindicated due to compromise of product integrity:

- **Adulterated Fill.** Do not place drugs or substances inside the implant other than sterile saline for injection.
- **Alteration.** Do not alter the implant or valve.
- **Do not inject** through the implant shell.
- **Stacking** of implants: Do not place more than one implant per breast.
- Do not allow the implant to come into contact with povidone iodine.

WARNINGS

1. Closed Capsulotomy

DO NOT treat capsular contracture by forceful external compression, which will likely result in implant damage, deflation, folds, and/or hematoma. Capsule firmness must not be treated by overexpansion of the device.

2. Reuse

Breast implants are intended for single use only. Do not resterilize.

3. Avoiding Damage during Surgery

- Care should be taken not to damage the prosthesis with surgical instruments.
- Do not insert or attempt to repair a damaged prosthesis.
- Use care in subsequent procedures such as open capsolotomy, breast pocket revision, hematoma/ seroma aspiration, and biopsy/lumpectomy to avoid damage to the implant shell or valve.
- Do not contact the implant with disposable, capacitor-type cautery devices.

4. Proper Filling

Follow the recommendation on the product data sheet for fill volume; do not overfill or underfill the implant. Following recommended fill volumes can decrease the possibility of shell wrinkling and crease fold failure.

5. Microwave Diathermy

The use of microwave diathermy in patients with breast implants is not recommended, as it has been reported to cause tissue necrosis, skin erosion, and extrusion of the implant.

6. Do not use endoscopic instruments or the periumbilical approach for placement of the implant as damage to the device may occur.

PRECAUTIONS

1. Specific Populations

Safety and Effectiveness has not been established in patients with:

- Autoimmune diseases such as lupus and scleroderma
- A compromised immune system (e.g., currently receiving immunosuppressive therapy)
- Patients with conditions or medications which interfere with wound healing ability (such as poorly controlled diabetes) or blood clotting (such as concurrent Coumadin® therapy).
- Reduced blood supply to breast tissue

2. Mammography

Breast implants may complicate the interpretation of mammographic images by obscuring underlying breast tissue and/or by compressing overlying tissue. Accredited mammography centers and use of displacement techniques are needed to adequately visualize breast tissue in the implanted breast. Presurgical mammography with a follow-up mammogram 6 months to 1 year following surgery may be performed to establish a baseline for future routine mammography.

3. Radiation to the Breast

INAMED has not tested the in vivo effects of radiation therapy in patients who have breast implants. The literature suggests that radiation therapy may increase the likelihood of capsular contracture, necrosis, and extrusion.

4. Long Term Effects

The long term safety and effectiveness of INAMED's breast implants have not been established. INAMED is monitoring the long term (i.e., 10 year) risk of implant rupture, reoperation, implant removal, and capsular contracture.

5. Instructions to Patients:

- ***Reoperation*** – Patients should be advised that additional surgery to their breast and/or implant will be likely over the course of their life.

- ***Explantation*** – Patients should be advised that implants are not considered life time devices and they will likely undergo implant removal, with or without replacement, over the course of their life. Patients should also be advised that the changes to their breast following explantation are irreversible.
- ***Mammography*** - Patients should be instructed to inform their mammographers about the presence of their implants.
- ***Lactation*** – Patients should be advised that breast implants may interfere with the ability to successfully breast feed.
- ***Breast Examination Techniques*** – Patients should be instructed to perform breast self-examinations monthly and be shown how to distinguish the implant from their breast tissue. The patient should be instructed not to manipulate (i.e., squeeze) the valve excessively, which may cause valve leakage.

Adverse Events

INAMED's Saline-Filled Breast Implants were evaluated in four major open label, multicenter clinical studies: the 1990 Augmentation/Reconstruction Study (AR90), the Large Simple Trial (LST, which involved 2875 patients), the 1995 Augmentation Study (A95, which involved 901 patients), and the 1995 Reconstruction Study (R95, which involved 237 patients). Because the AR90 Study utilized devices and surgical practices that are not current, these data are not reported below. The cumulative Kaplan-Meier risk of first occurrence of adverse events (and 95% confidence interval) reported in greater than 1% of patients is shown in Tables 1 and 2 based on indication.

Table 1
LST: 1-Year Cumulative First Occurrence Kaplan-Meier Adverse Event Risk Rates (95% Confidence Interval), By Patient

Complication	Augmentation		Reconstruction		Revision	
	Rate (%)	(95% CI)	Rate (%)	(95% CI)	Rate (%)	(95% CI)
Capsular Contracture III/IV	7.2	(5.8, 8.6)	12.5	(7.3, 17.8)	11.8	(7.1, 16.4)
Implant Removal with or without Replacement	6.1	(4.9, 7.3)	13.7	(8.7, 18.6)	7.8	(4.2, 11.5)
Leakage/Deflation	3.6	(2.6, 4.5)	2.6	(0.0, 5.2)	5.4	(2.0, 8.8)
Infection	1.5	(0.9, 2.1)	6.2	(2.9, 9.5)	3.3	(1.1, 5.6)

Table 2
A95/R95: 3-Year** and 5-Year Cumulative First Occurrence Kaplan-Meier Adverse Event Risk Rates (95% Confidence Interval), By Patient

Complication	Augmentation (N = 901)				Reconstruction (N = 237)			
	3-Year		5-Year		3-Year		5-Year	
	Rate (%)	(95% CI)	Rate (%)	(95% CI)	Rate (%)	(95% CI)	Rate (%)	(95% CI)
Reoperation	21.1	(18.4, 23.8)	25.9	(23.0, 28.9)	38.7	(32.3, 45.0)	44.5	(37.9, 51.0)
Breast Pain*	15.6	(13.2, 17.9)	17.0	(14.5, 19.5)	15.3	(10.3, 20.2)	17.7	(12.4, 23.0)
Wrinkling*	10.5	(8.4, 12.6)	13.7	(11.3, 16.1)	23.3	(17.5, 29.1)	24.6	(18.6, 30.6)
Asymmetry*	10.1	(8.1, 12.1)	12.2	(10.0, 14.4)	33.0	(26.6, 39.4)	39.0	(32.1, 45.8)
Nipple Paresthesia*	9.3	(7.4, 11.2)	9.8	(7.8, 11.8)	<1	<1	<1	(0.0, 1.2)
Implant Palpability/Visibility*	9.2	(7.2, 11.1)	12.1	(9.8, 14.3)	20.0	(14.5, 25.5)	27.1	(20.6, 33.5)
Capsular Contracture III/IV or grade unknown	8.7	(6.8, 10.6)	11.4	(9.2, 13.5)	25.3	(19.5, 31.2)	35.7	(29.0, 42.4)
Loss of Nipple Sensation*	8.4	(6.5, 10.2)	9.9	(7.8, 11.9)	12.0	(7.4, 16.6)	18.1	(12.5, 23.8)
Implant Malposition*	8.2	(6.3, 10.0)	9.2	(7.3, 11.2)	12.2	(7.8, 16.6)	16.9	(11.7, 22.2)
Implant Removal for Any Reason	7.6	(5.8, 9.4)	11.8	(9.6, 14.0)	22.5	(17.1, 28.0)	28.0	(22.1, 34.0)
Skin Paresthesia*	7.2	(5.5, 9.0)	7.6	(5.9, 9.4)	5.6	(2.5, 8.6)	6.3	(2.9, 9.6)
Scarring Complications	6.4	(4.8, 8.0)	6.5	(4.9 8.2)	6.0	(2.7, 9.2)	6.0	(2.7, 9.2)
Leakage/Deflation	5.0	(3.5, 6.4)	6.8	(5.0, 8.5)	6.2	(2.9, 9.5)	7.5	(3.8, 11.2)
Irritation/Inflammation*	2.9	(1.8, 4.0)	3.2	(2.0, 4.3)	6.6	(3.3, 9.8)	6.6	(3.3, 9.8)
Seroma	2.6	(1.6, 3.7)	2.6	(1.6, 3.7)	3.9	(1.4, 6.4)	3.9	(1.4, 6.4)
Hematoma	1.6	(0.7, 2.4)	1.7	(0.8, 2.5)	1.3	(0.0, 2.8)	1.3	(0.0, 2.8)
Skin Rash	1.6	(0.8, 2.4)	1.9	(1.0, 2.8)	3.3	(0.9, 5.7)	3.3	(0.9, 5.7)
Capsular Calcification*	1.2	(0.4, 1.9)	1.8	(0.9, 2.7)	4.7	(1.9, 7.6)	5.4	(2.3, 8.6)
Infection	<1	<1	1.0	(0.3, 1.6)	4.8	(2.0, 7.5)	6.0	(2.8, 9.2)
Delayed Wound Healing*	<1	<1	<1	<1	2.7	(0.6, 4.9)	2.7	(0.6, 4.9)
Implant Extrusion	<1	<1	<1	<1	2.6	(0.6, 4.7)	3.2	(0.9, 5.6)
Tissue/Skin Necrosis	<1	<1	<1	<1	3.6	(1.1, 6.0)	3.6	(1.1, 6.0)

* These complications were assessed with severity ratings. Only the rates for moderate, severe, or very severe (excludes mild and very mild ratings) are shown.

** 3-year risk rates as reported in original PMA submission.

46

Of the 901 patients in the A95 Study, at least one additional surgical procedure was performed on 204 patients (23%) through 4 years and 224 patients (25%) through 5 years. A total of 402 surgical procedures were performed through 4 years and 463 procedures were performed through 5 years in the A95 Study.

Of the 237 patients in the R95 Study, at least one additional surgical procedure was performed on 171 patients (72%) through 4 years, involving 433 surgical procedures. Most of the 433 procedures were planned nipple reconstruction and nipple/areolar tattoo procedures. In terms of unplanned procedures, a total of 151 procedures were performed through 4 years and 159 procedures were performed through 5 years in the R95 Study.

Table 3 shows the types of additional surgical procedures performed through 4 and 5 years in the A95/R95 Studies based on the total number of additional surgical procedures.

Table 3
A95/R95: Types of Additional Surgical Procedures through 4 Years* and 5 Years

Type of Additional Surgical Procedures	Augmentation*				Reconstruction*			
	Through 4 Years N = 402		Through 5 Years N = 463		Through 4 Years N = 151		Through 5 Years N = 159	
	n	percent	n	percent	n	percent	n	percent
Implant Removal w/Replacement**	122	30	156	34	45	30	49	31
Capsule Related**	78	19	86	19	18	12	13	8
Add/Remove Saline	46	11	49	11	9	6	10	6
Scar Revision/Wound Repair	36	9	42	9	29	19	30	19
Mastopexy	28	7	28	6	0	0	0	0
Aspiration	28	7	29	6	7	5	7	4
Reposition Implant	19	5	20	4	6	4	7	4
Biopsy/Lump Removal	16	4	21	5	7	5	7	4
Implant Removal without Replacement	10	3	10	2	17	11	21	13
Exploration of Breast Area or Implants	8	2	6	1	0	0	0	0
Removal of Skin Lesion or Cyst	6	2	10	2	1	1	3	2
Skin Related Procedure	4	1	3	1	6	4	6	4
Unplanned Nipple-Related Procedure	1	<1	1	<1	3	2	3	2
Other Procedures****	0	0	0	0	3	2	3	2

* As reported in original PMA submission with additional data clarification.
** Capsule related includes capsulectomy, capsulotomy, and capsulorraphy.
*** Some removals were replaced with an Inamed implant, while others were replaced with a non-Inamed implant.
**** Other procedures through 5 years include liposuction, and placement of a stacked implant.

Of the 901 patients in the A95 Study, at least one reoperation was performed on 204 patients (23%) through 4 years, and 225 patients (25%) through 5 years. A total of 257 reoperations were performed through 4 years, and 293 through 5 years in the A95 Study. The primary reason for reoperation through 5 years was implant deflation at 18.1%.

Of the 237 patients in the R95 Study, at least one reoperation was performed on 94 patients (40%) through 4 years, and 99 patients (42%) through 5 years. A total of 117 reoperations were performed through 4 years, and 125 through 5 years in the R95 Study. The primary reason for reoperation through 5 years was capsular contracture at 27.2%.

Table 4 shows the reasons for reoperation through 4 and 5 years in the A95/R95 Studies based on the total number of reoperations.

Table 4
A95/R95: Reasons for Reoperation Through 4 Years and 5 Years

Reasons for Reoperation	Augmentation				Reconstruction			
	Through 4 Years N = 257		Through 5 Years N = 293		Through 4 Years N = 117		Through 5 Years N = 125	
	n	percent	n	percent	n	percent	n	percent
Capsular Contracture	47	18.3	52	17.7	31	26.5	34	27.2
Leakage/Deflation	45	17.5	53	18.1	9	7.7	11	8.8
Patient Choice	38	14.8	45	15.3	13	11.1	13	10.4
Hematoma/Seroma	25	9.7	26	8.9	6	5.1	6	4.8
Implant Malposition	24	9.3	28	9.6	12	10.3	11	8.8
Lump/Mass/Cyst	20	7.8	25	8.5	9	7.7	10	8.0
Scarring	18	7.0	21	7.2	10	8.5	10	8.0
Ptosis	14	5.4	17	5.8	0	0.0	0	0.0
Asymmetry	13	5.1	14	4.8	25	21.4	25	20.0
Add/Remove Saline	12	4.7	14	4.7	4	3.5	4	3.2
Wrinkling	8	1.9	8	2.7	3	2.6	5	4.0
Unsatisfactory Nipple Result	4	1.6	5	1.7	1	0.9	1	0.8
Delayed Wound Healing	4	1.6	4	1.4	2	1.7	2	1.6
Skin Lesion/Cyst	3	1.2	3	1.0	1	0.9	2	1.6
Infection	3	1.2	4	1.4	8	6.8	9	7.2
Implant Palpability	2	0.8	4	1.4	2	1.7	3	2.4
Breast Pain	2	0.8	2	0.7	6	5.1	9	4.8
Irritation	1	0.4	1	0.3	0	0.0	0	0.0
Implant Extrusion	1	0.4	1	0.3	5	4.3	5	4.0
Tissue/Skin Necrosis	0	0.0	0	0.0	6	5.1	6	4.8
Suture/Incision Observation	0	0.0	0	0.0	0	0.0	0	0.0
Capsule Calification	0	0.0	1	0.3	0	0.0	0	0.0
Total	**281**	**109.3***	**328**	**111.9***	**153**	**130.8***	**163**	**130.4***

*Total is greater than 100% because some reoperations were performed for multiple reasons.

50

Of the 901 augmentation patients in A95, there were 81 patients (9.0%) who had 132 implants removed through 4 years. A total of 98 patients had 166 implants removed through 5 years. Of the 237 reconstruction patients in R95, there were 58 patients (24.5%) who had 62 implants through 4 years. A total of 62 patients had 70 implants removed through 5 years. Of the 166 augmentation implants removed through 5 years, 94% were replaced; of the 70 reconstruction implants removed through 5 years, 70% were replaced. The primary reason for implant removal is shown in Table 5 below based on the number of implants removed.

Table 5
A95/R95: Reasons for Implant Removal Through 4 Years* and 5 Years

Primary Reason for Implant Removal	Augmentation				Reconstruction			
	Through 4 Years N = 132		Through 5 Years N = 166		Through 4 Years N = 62		Through 5 Years N = 70	
	n	percent	n	percent	n	percent	n	percent
Patient Choice	57	43	72	43	14	23	15	21
Leakage/Deflation**	44	33	54	33	10	16	12	17
Capsular Contracture	13	10	17	10	16	26	22	31
Wrinkling	6	5	6	1	2	3	2	3
Asymetry	4	3	3	2	2	3	1	1
Breast Pain	3	2	3	2	0	0	0	0
Malposition	2	2	2	1	4	6	3	4
Iatrogenic Injury	1	1	1	1	0	0	0	0
Infection	1	1	1	1	6	10	7	10
Implant Extrusion	1	1	1	1	4	6	4	6
Implant Palpability/Visibility	0	0	6	4	0	0	0	0
Recurrent Breast Cancer	0	0	0	0	2	3	1	1
Other***	0	0	0	0	2	3	3	4
Total	**132**	**100**	**166**	**100**	**62**	**100**	**70**	**100**

* As reported in original PMS submission with some data recategorization of "Other".

** Includes unreported unknown (n=1 augmentation through 5 years, n=1 reconstruction through 4 years, n=2 reconstruction through 5 years).

*** Reconstruction: Through 4 years, other reasons were: abnormality of CT scan at mastectomy site (n=1), poor tissue expansion due to radiation (n=1). Through 5 years, other reasons were: abnormality of CT scan at mastectomy site (n=1), poor tissue expansion due to radiation (n=1), second stage breast reconstruction (n=1).

Potential Adverse Events

The following is a list of potential adverse events that may occur with breast implant surgery. Some of these adverse events have been reported in tables 1 and 2 above. The risks include: implant deflation/ leakage, additional surgery, capsular contracture, infection, Toxic Shock Syndrome, necrosis, hematoma, seroma, extrusion, breast pain, changes in nipple sensation, changes in breast sensation, dissatisfaction with cosmetic results (wrinkling, folding, displacement, asymmetry, palpability, visibility, ptosis, sloshing), calcific deposits, irritation/inflammation, delayed wound healing, hypertrophic scarring, breast tissue atrophy/chest wall deformity, difficulty/inability in breast feeding, and inability to adequately visualize breast lesions with mammography. In addition to these potential adverse events, there have been concerns with certain systemic diseases.

- **Connective Tissue Disease**
  Concern over the association of breast implants to the development of autoimmune or connective tissue diseases, such as lupus, scleroderma, or rheumatoid arthritis, was raised because of cases reported in the literature with small numbers of women with implants. A review of several large epidemiological studies of women with and without implants indicates that these diseases are no more common in women with implants than those in women without implants.

- **Cancer**
  Published studies indicate that breast cancer is no more common in women with implants than those without implants.

- **Second Generation Effects**
  There have been concerns raised regarding potential damaging effects on children born of mothers with implants. A review of the published literature on this issue suggests that the information is insufficient to draw definitive conclusions.

CLINICAL STUDIES OVERVIEW

1. Study Design

The safety and effectiveness of INAMED's Saline-Filled Breast Implants were evaluated in four open label, multicenter clinical studies: the 1990 Augmentation/Reconstruction Study (AR90), the Large Simple Trial (LST), the 1995 Augmentation Study (A95), and the 1995 Reconstruction Study (R95). Patients studied were those seeking implant surgery for augmentation or reconstruction of the breast. Because the 1990 Study utilized devices and surgical practices which are not current, these data are not reported below. The LST Study was designed as a one year study to assess the four safety outcomes of capsular contracture, infection, implant leakage/deflation, and implant removal for a large number of patients.

The A95/R95 Studies were designed as 5 year studies to assess safety and effectiveness. Patient follow-up was yearly for 5 years. Safety assessments in the A95/R95 Studies consisted of adverse event rates and rates of secondary surgical treatment. Effectiveness assessments in the A95/R95 Studies consisted of patient satisfaction, breast size change, and measures of body esteem/self esteem/body image. A95/R95 data through 3 years (with partial 4 year data) was presented to FDA for PMA approval. After PMA approval, INAMED transitioned data collection to a post-approval study. The first phase of this post-approval study consisted of completion of the A95 and R95 Studies, with collection of all risk/benefit information through 5 years post-implant. The second phase of the post-approval study consists of a patient survey-based study, with collection of specific risk/benefit information through 6-10 years post implant.

The data presented to FDA for PMA approval (i.e., 4-year data) along with post-approval data through 5 years and 7 years are included in this brochure. Please note that the data/tables labeled "through 4 years" are only partial 4-year study data as reported in the original PMA or current FDA-approved labeling.

2. Patient Accounting and Baseline Demographic Profile

The LST Study enrolled 2,333 augmentation patients, 225 reconstruction patients, and 317 revision patients with an overall 1-year follow-up compliance rate of 62%. The A95 Study enrolled 901 augmentation patients, with 77% returning for their 3-year follow-up visit. Of those A95 patients available to be seen for their 5-year follow-up visit, 81% returned and were seen at 5 years after implant surgery. The R95 Study enrolled 237 reconstruction patients, with 71% returning for their 3-year follow-up visit. Of those R95 patients available to be seen for their 5-year follow-up visit, 80% returned and were seen at 5 years after implant surgery. Demographic

information obtained from the 1995 Studies revealed that nearly 90% of both augmentation and reconstruction patients were Caucasian and more than half of study participants were married. The median age of the augmentation patients was 32 years (range: 19-66); for reconstruction patients the median age was 47 years (range: 25-77). With respect to surgical baseline factors in the 1995 Studies, for augmentation patients, the most frequently used devices were textured round, the most common incision sites were periareolar and inframammary, and the most frequent placement of the implant was submuscular. For reconstruction patients, the most frequently used devices were textured BioDIMENSIONAL®, the most common incision site was the mastectomy scar, and the most frequent placement of the implant was submuscular.

3. Safety Outcomes

The LST safety outcomes are presented in Table 1 above. The A95 Study and R95 Study safety outcomes for primary implantation are presented in Tables 2–4 above. As additional safety information, Tables 5a and 5b below show the 2-year and 3-year cumulative Kaplan-Meier adverse event risk rates of first occurrence following implant replacement (i.e., revision) on a by implant basis for the A95 and R95 Studies. There were 126 augmentation implants and 40 reconstruction implants in the A95/R95 Studies that were removed and replaced with INAMED study devices.

Table 5a
A95: 2-Year* and 3-Year Cumulative First Occurrence Kaplan-Meier Adverse Event Risk Rates (95% Confidence Interval) Following Augmentation Implant Replacement, by Implant

Complication Following Replacement of Augmentation Implants	2-Year Risk Rate* N = 108 Implants		3-Year Risk Rate N = 126 Implants	
	%	95% CI	%	95% CI
Removal/Replacement	5.4	(0.2, 10.5)	18.3	(9.4, 27.1)
Leakage/Deflation	9.1	(3.4, 14.7)	9.3	(3.1, 15.6)
Capsule Contracture III/IV	7.3	(1.5, 13.0)	7.6	(2.5, 12.7)
Infection	1.0	(0.0, 3.0)	2.5	(0.0, 5.3)

* As reported in original PMA submission with additional data clarification.

54

Table 5b

R95: 2-Year* and 3-Year Cumulative First Occurrence Kaplan-Meier Adverse Event Risk Rates (95% Confidence Interval) Following Reconstruction Implant Replacement, by Implant

Complication Following Replacement of Reconstruction Implants	2-Year Risk* Rate N = 40 Implants		3-Year Risk Rate N = 40 Implants	
	%	95% CI	%	95% CI
Capsule Contracture III/IV	32.6	(16.6, 48.5)	33.8	(18.0, 49.5)
Removal/Replacement	25.5	(9.8, 41.3)	26.9	(12.5, 41.2)
Leakage/Deflation	5.3	(0.0, 12.5)	9.5	(0.0, 20.1)
Infection	7.3	(0.0, 17.3)	2.9	(0.0, 8.4)

* As reported in original PMA submission with correction of capsular contracture rate.

CTD and Breast Disease

Tables 6a and 6b summarize post-implant observations from the A95 and R95 Studies pertaining to connective tissue/autoimmune (CTD) disease and breast disease (including breast carcinoma). These data should be interpreted with caution in that there was no comparison group of similar women without implants. Unconfirmed reports were based on self-reports by the patients. Confirmed reports were based on a diagnosis by a physician. Data pertaining to effects on offspring and mammographic detection of tumors/lesions were not collected in these studies. From 4 to 5 years, the total number of confirmed CTD and breast disease reports has changed due to the identification of new reports, the removal of unconfirmed reports found to be false, and/or the recategorization of reports between the 4th and 5th year. With regard to CTD, from 4 to 5 years, there have been 11 new reports (2 confirmed, 9 unconfirmed) among the augmentation patients and 4 new reports (all unconfirmed) among the reconstruction patients. With regard to breast disease, from 4 to 5 years, there have been 7 new reports among the augmentation patients and 7 new reports among the reconstruction patients.

Table 6a
A95/R95: Reports of CTD Through 4 Years* and 5 Years, By Patient

Rheumatic Disease	Augmentation				Reconstruction			
	Through 4 Years		Through 5 Years		Through 4 Years		Through 5 Years	
	No. of Confirmed Reports	No. of Unconfirmed Reports	No. of Confirmed Reports	No. of Unconfirmed Reports	No. of Confirmed Reports	No. of Unconfirmed Reports	No. of Confirmed Reports	No. of Unconfirmed Reports
Graves' Disease	2	0	3	0	1	0	1	0
Hyperthyroiditis	1	2**	2	1	0	0	0	0
Inflammatory Bowel Disease	0	0	0	1	0	1	0	0
Lupus Erythematosus and/or Rheumatoid Arthritis	0	3	0	1	0	1	0	3
Thyroiditis	0	2	0	4	0	2	0	1
Chronic Fatigue Syndrome or Fibromyalgia	2	0	2	4	0	0	0	0
Seronegative Spondylarthritis	0	0	0	1	0	0	0	0
Raynaud's Phenomenon, Graves' Disease, Hyperthyroiditis, and Rheumatoid Arthritis	0	0	0	1**	0	0	0	0
Total	**5**	**7**	**7**	**13**	**1**	**4**	**1**	**4**

*As reported in original PMA submission.

**Patient was recategorized at 5-year timepoint.

56

Table 6b
A95/R95: Reports of Breast Disease 4 Years* and 5 Years, By Patient

Breast Disease Observation	Augmentation		Reconstruction	
	Through 4 Years n	Through 5 Years n	Through 4 Years n	Through 5 Years n
Benign	66	80	72	75
Malignant	1	1	19	24
Unknown Outcome	7	0	1	0

* As reported in original PMA submission with additional data clarification:
Benign includes 22 additional augmentation reports and 61 additional reconstruction reports, and unknown outcome includes 2 fewer augmentation reports.

4. Effectiveness Outcomes

Effectiveness of saline-filled breast implants was assessed by a variety of outcomes, including bra cup size change (augmentation patients only), patient satisfaction, body image, body esteem, and self concept. These outcomes were assessed for patients with both original and replacement saline devices before implantation and at 3 years after surgery, except for bra size and satisfaction. Bra size was measured within the first year and a half after surgery. Satisfaction was measured at every follow-up visit through 5 years.

Augmentation
859 of the original 901 augmentation patients (95%) at 18 months were included in an analysis of cup size (5% did not provide data because pre/post measurements were not obtained or replacement/ removal occurred prior to obtaining a post measurement). Of these 859 patients, the following shows the percentage of patients experiencing various changes in cup size:

- Increase by 1 cup size: 38%
- Increase by 2 cup sizes: 49%
- Increase by 3 cup sizes: 9%
- No Increase: 4%

683 of the original 901 augmentation patients (76%) were included in an analysis of satisfaction at 5 years (24% were not included because satisfaction data was not obtained or implant replacement/ removal occurred prior to 5 years). Of these 683 patients, 95% indicated being satisfied with their breast implants at 5 years. Before implantation, augmentation patients scored higher (better) than the general U.S. female population on the SF-36 and MOS-20 scales, which measure general health-related quality of life. After 3 years, augmentation patients showed a worsening in their SF-36 and MOS-20 scores. The following two scales showed no change over the 3 years: The Tennessee Self Concept Scale (which measures overall self concept) and The Body Esteem Scale (which measures overall self esteem related specifically to one's body). The Rosenberg Self Esteem Scale (which measures overall self esteem) showed a slight improvement over the 3 years. The Semantic Differential Scale (which measures attitudes about your breasts compared to attitudes about yourself) showed that patients experienced an increased positive attitude towards their breasts compared to themselves over the 3 years.

Reconstruction

137 of the original 237 reconstruction patients (58%) were included in an analysis of satisfaction at 5years (42% were not included because satisfaction data was not obtained or implant replacement/ removal occurred prior to 5 years). Of these 137 patients, 89% indicated being satisfied with their breast implants at 5 years. Before implantation, reconstruction patients scored higher (better) than the general U.S. female population before implantation on some SF-36 scales, which measure general health-related quality of life. After 3 years, reconstruction patients showed an improvement in some of their SF-36 and MOS- 20 scores. The following three scales showed no change over the 3 years: The Tennessee Self Concept Scale (which measures overall self concept), The Rosenberg Self Esteem Scale (which measures overall self esteem), and The Body Esteem Scale (which measures overall self esteem related specifically to one's body). The Semantic Differential Scale (which measures attitudes about your breasts compared to attitudes about yourself) showed that patients experienced an increased positive attitude towards their breasts compared to themselves over the 3 years.

Post-Approval Study

The post-approval study transitioned patients from data collection via physicians (0-5 years post-implantation) to data collection via mailed patient-completed surveys (6-10 years post-implantation). The tables below present data collected through 7 years post-implantation. 85% of the augmentation patients and 83% of the reconstruction patients expected for follow-up at 7 years returned surveys to INAMED according to study protocol. The surveys at 7-years showed 88% of the augmentation patients and 88% of the reconstruction patients who provided satisfaction scores indicated being satisfied with their breast implants at 7 years post-implant. The cumulative Kaplan-Meier risk of first occurrence of adverse events (and 95% C.I.) are shown in Table 7 below.

Table 7
Post Approval: 7 Year First Occurrence Kaplan-Meier Adverse Event Risk Rates (95% Confidence Interval), By Patient

Complication	7-Year Risk			
	Augmentation (N = 901)		Reconstruction (N = 237)	
	Rate (%)	(95% CI)	Rate (%)	(95% CI)
Reoperation	29.9	(26.8, 32.9)	48.0	(41.4, 54.7)
Breast Pain	24.5	(21.5, 27.4)	25.9	(19.5, 32.3)
Capsular Contracture	15.7	(13.2, 18.2)	42.6	(35.6, 49.6)
Implant Removal	14.5	(12.2, 16.9)	31.3	(24.1, 37.5)
Implant Deflation	9.8	(7.8, 11.9)	12.4	(7.6, 17.2)

Of the 901 augmentation patients in the PASS Study, at least one reoperation was performed on 261 patients (29%) through 7 years. A total of 343 reoperations were performed. The primary reason for reoperation through 7 years on augmentation patients was implant deflation at 19.2%.

Of the 237 reconstruction patients in the PASS Study, at least one unplanned reoperation was performed on 107 patients (45.1%) through 7 years. A total of 138 unplanned reoperations were performed. The primary reason for reoperation through 7 years on reconstruction patients was capsular contracture at 25.4%.

Table 8 shows the reasons for reoperation through 7 years in the PASS Study based on the total number of reoperations.

59

Table 8
Post Approval: Reasons for Reoperation Through 7 Years

Reasons for Reoperation	7-Year Augmentation (N = 343 Reoperations)		7-Year Reconstruction (N = 138 Reoperations)	
	n	%	n	%
Implant Deflation	66	19.2	16	11.6
Patient Choice	61	17.8	16	11.6
Capsular Contracture	54	15.7	35	25.4
Lump/Mass/Cyst	43	12.5	12	8.7
Implant Malposition	30	8.7	13	9.4
Hemotoma/Seroma	27	7.9	6	4.3
Scarring	22	6.4	11	8.0
Ptosis	21	6.1	1	0.7
Add/Remove Saline	18	5.3	4	2.9
Asymmetry	14	4.1	25	18.1
Wrinkling	8	2.3	5	3.6
Implant Palpability	5	1.5	3	2.2
Unsatisfactory Nipple Result	5	1.5	2	1.4
Delayed Wound Healing	4	1.2	2	1.4
Infection	4	1.2	9	6.5
Skin Lesion/Cyst	3	0.9	2	1.4
Breast Pain	2	0.6	6	4.3
Capsule Calcification	1	0.3	0	0.0
Implant Extrusion	1	0.3	5	3.6
Irritation	1	0.3	0	0.0
Cancer	0	0.0	1	0.7
Tissue/Skin Necrosis	0	0.0	6	4.3
Total	**390**	**113.8**	**180**	**130.1**

* Some reoperations were performed for multiple reasons; all reasons are included in this table.

The main reasons for implant removal through 7 years are shown in Table 9 below. Through 7 years, 213 implants were removed from 124 augmentation patients and 81 implants were removed from 69 reconstruction patients.

Table 9
Post Approval: Reasons for Implant Removal Through 7 Years

Primary Reason for Implant Removal	Augmentation Through 7 Years N = 213		Reconstruction Through 7 Years N = 81	
	n	percent	n	percent
Patient Choice	90	42.3	19	23.5
Implant Deflation	68	31.9	20	24.7
Capsular Contracture	20	9.4	20	24.7
Wrinkling	8	3.8	2	2.5
Implant Malposition	8	3.8	3	3.7
Implant Palpability/Visibility	6	2.8	0	0.0
Asymmetry	6	2.8	2	2.5
Breast Pain	3	1.4	0	0.0
Iatrogenic Injury	1	0.5	0	0.0
Infection	1	0.5	7	8.6
Implant Extrusion	1	0.5	4	4.9
Breast Mass/Lump/Cyst	1	0.5	0	0.0
Hemotoma	0	0.0	0	0.0
Other*	0	0.0	4	4.9
Total	**213**	**100.1**	**81**	**100.0**

* Other reasons as reported by the physician were: Recurrent Carcinoma (n-=1), Abnormality on CT Scan at Mastectomy Site (n=1), Tissue expansion went poorly due to radiation (n=1), Second stage breast Recon (n=1).

INSTRUCTIONS FOR USE

NOTE: Back-up breast implants must be available during the procedure.

DO NOT Stack more than one implant per breast.

Single Use

This product is intended for **single use only**. Do not reuse explanted implants.

Product Identification

Product labels accompany each device within the internal product packaging. The product labels provide product-specific information. Product labels may be attached to the patient's chart for identification purposes. The Device Identification Card should be provided to the patient for personal reference.

Surgical Planning

Proper surgical planning such as allowance for adequate tissue coverage, implant site (i.e., submuscular vs. subglandular), incision site, implant type etc. should be made preoperatively. The surgeon must carefully evaluate implant size and contour, incision placement, pocket dissection, and implant placement criteria, with respect to the patient's anatomy and desired physical outcome. Planning should include clear delineation of aesthetic goals to ensure mutual understanding between surgeon and patient.

Sterile Product

Each sterile saline-filled breast implant is supplied in a sealed, double primary package. Style-specific sterile product accessories are also supplied within the product packaging. Sterility of the implant is maintained only if the thermoform packages, including the package seals, are intact. Use standard procedures to maintain sterility during transfer of the breast implant to the sterile field. Remove the breast implant and accessories from their packages in an aseptic environment and using talc-free gloved hands.

DO NOT use the product if the thermoform packages or seals have been damaged.

DO NOT implant damaged or contaminated breast implants.

DO NOT store the breast implant with the fill tube in place, which may damage the integrity of the valve seal.

DO NOT resterilize the product.

NEVER, under any circumstances, attempt to resterilize using ethylene oxide, which is known to cause adverse tissue reaction if not completely removed from the device. Avoid unnecessary exposure of the breast implant to lint, talc, sponge, towel, skin oils, and other contaminants. Prior to use, keep the breast implant in the inner thermoform and covered to prevent contact with airborne and surgical field particulate contaminants.

1. Peel open the lid of the outer thermoform package.

2. Invert the outer thermoform over the sterile field, allowing the sealed inner thermoform to gently fall into the field.

3. Peel open the lid of the inner package using the pull tab.

4. Gently retrieve the breast implant.

Surgical Procedure

Breast augmentation with saline-filled implants can be carried out through several different incisions including inframammary, periareolar, or transaxillary. The transumbilical incisional approach is not recommended. Some surgeons advocate a "no-touch" technique, which requires significant attention to minimizing contact between the patient's skin and the implant.

Pocket dissection should be planned out preoperatively and be performed accurately and with minimal trauma. Excellent hemostasis is important to avoid postoperative hematoma. The implant may be placed subglandularly or subpectorally depending upon the balance of cosmetic and medical considerations in any given patient. The size and shape of the device may be determined preoperatively by means of dimensional planning or intraoperatively with the help of temporary sizer devices. The implant may be filled with saline either before or after insertion. If inserted without saline, the implant may be inserted as received (i.e., filled with air), or the air may be evacuated prior to insertion. Regardless of which insertion technique is used, it is important to ultimately evacuate as much air from the implant as possible. It is also important to maintain proper orientation of any BioDIMENSIONAL® implant. The incision for the placement of the implant should be securely closed and in several layers, whenever possible. Drains are optional.

Breast Reconstruction is generally carried out in the mastectomy scar. Special care must be used in breast reconstruction to make sure that appropriate amounts of healthy tissue be available to cover the

implant and that the implant be properly sized and positioned based upon careful preoperative planning. Educational materials are available through the Inamed Customer Care Department to supplement surgical knowledge of the dimensional techniques intended for use with BioDIMENSIONAL® styles.

Maintaining Hemostasis/Avoiding Fluid Accumulation

Postoperative hematoma and seroma may be minimized by meticulous attention to hemostasis during surgery, and possibly also by postoperative use of a closed drainage system. Persistent, excessive bleeding must be controlled before implantation. Any postoperative evacuation of hematoma or seroma must be conducted with care to avoid breast implant contamination, or damage from sharp instruments.

Technique for Using Breast Implants with Diaphragm Valve

The fill volume range is specified on the product package labeling and data sheet. Following recommended fill volumes can decrease the possibility of shell wrinkling and crease fold failure.

DO NOT underfill or overfill the breast implant beyond the range specified.

DO NOT use excessive force during any of the steps in the following procedure.

DO NOT damage the breast implant with sharp surgical instruments such as needles and scalpels, or by excessive handling and manipulation during introduction into the surgical pocket.

1. Fill tube insertion

Prepare the fill tube by attaching the reflux valve to the Luer adapter of the fill tube as shown in **Figure 1.** The reflux valve prevents back-flow during intraoperative filling. This two-way valve opens when a syringe is attached, and closes when the syringe is removed.

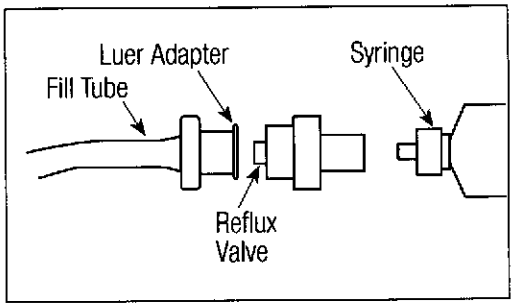

Figure 1

Figure 2 shows a cross section of the diaphragm valve with the strap closure in place and the valve closed. To insert the fill tube, wet the tip of the fill tube in sterile saline for injection and push the strap closure to one side of the valve entrance.

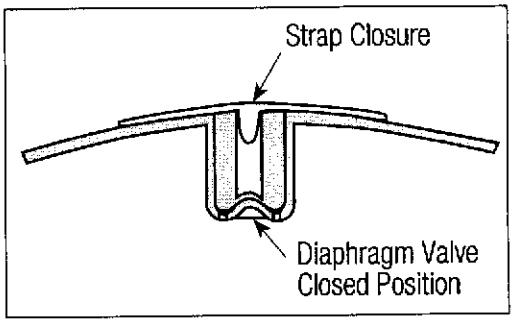

Figure 2

Insert the fill tube by gently pushing the fill tube tip into the valve entrance. Do not use excessive force while inserting the fill tube tip. When the fill tube flange nears or makes contact with the implant shell, the fill tube is in the proper position and the diaphragm valve is open (**Figure 3**).

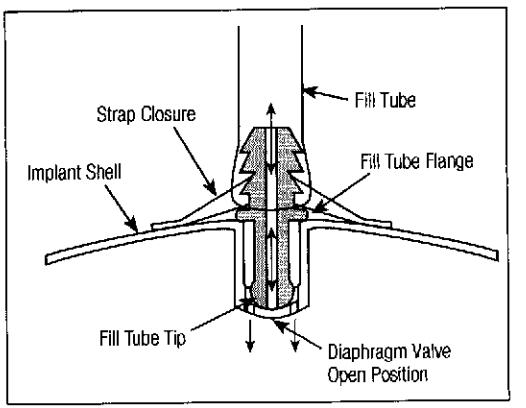

Figure 3

2. *Air aspiration*

After the fill tube is properly inserted, remove any air from the breast implant by aspiration with an empty sterile syringe attached to the reflux valve on the fill tube.

3. *Placement*

To assist with placement, a sterile BIOCELL® Delivery Assistance Sleeve is available separately. Use of this sleeve for insertion of BIOCELL® textured breast implants provides a shell/tissue interface with less friction. Insert the breast implant into one end of the sleeve. Insert the proximal end of the sleeve into the surgically-prepared pocket. With the tissue retracted, the sleeve can be twisted at its distal end to gently guide the breast implant into the pocket. Once the implant is inserted, gently remove the sleeve, and verify the correct orientation of the valve and the implant.

DO NOT use lubricants to facilitate placement, which create the risk of pocket contamination.

Lubricants may also affect tissue adherence.

DO NOT use the breast implant for expansion or dissection of the pocket.

4. *Filling*

Use a syringe filled with sterile, pyrogen-free Sodium Chloride U.S.P. Solution for Injection to fill the prosthesis and fill to a volume within the recommended fill range specified on the product package labeling and data sheet. Only sterile pyrogen-free Sodium Chloride U.S.P. Solution for Injection drawn from its original container should be used. As it is known that bacterial infections may result from contaminated saline, it is recommended that a new sterile saline container be used with each surgery and implant-filling procedure.

NOTE: The order of filling, placement, and orientation may vary with surgeon preference and technique.

5. *Residual Air*

After filling is completed, aspirate any residual air bubbles. Then use gentle traction to remove the fill tube from the valve, taking care to avoid damage to shell or valve.

6. *Diaphragm Valve Closure*

Use gentle traction to remove the fill tube from the valve, taking care to avoid damage to shell or valve. Verify that the diaphragm valve is clear of particulates. Once the fill tube tip is removed the diaphragm valve is closed. To help retard tissue ingrowth or fluid accumulation in the valve entrance, engage the strap closure as follows: using the thumb and forefinger, compress the valve seat and the strap to snap the valve plug into place as shown in **Figure 2.**

Information a Physician Should Provide to the Patient

Breast implantation is an elective procedure and the patient must be well counseled on the risk-benefit relationship. The surgeon should provide each prospective patient with the following:

- Making an Informed Decision

  This brochure can be used to facilitate patient education in the risks and benefits of saline-filled breast implant surgery. The patient should be advised to wait a week after reviewing and considering this information before deciding whether to have augmentation surgery.

- Device Identification Card

  Enclosed with each saline-filled breast implant is a Device Identification Card. To complete the Device Identification Card, place one device identification sticker for each implant on the back of the card. Stickers are located on the internal product packaging attached to the label. If a sticker is unavailable, the lot number, catalog number and description of the device may be copied by hand from the device label. Patients should be provided with these cards for personal reference.

Specific Product Information

BIOCELL® Delivery Assistance Sleeve

Sterile BIOCELL® Delivery Assistance Sleeves are available from your INAMED Aesthetics Sales Representative or Customer Care Department at 800.766.0171.

Returned Goods Policy

Product returns should be handled through a INAMED Aesthetics Sales Representative or through the Customer Care Department at 800.766.0171. Return value is based on time limitations. All package seals must be intact to be eligible for return. Returned products may be subject to a restocking charge. Certain products are non-returnable, including Zyderm® and Zyplast®.

Reporting and Return of Explanted Devices

The reason for explantation should be reported and the explanted device returned to INAMED Corporation. In the event of such an explantation, please contact Product Support at 800.624.4261 for an Explant Kit and explant return instructions.

ConfidencePlus™ Limited Warranties

The ConfidencePlus™ Limited Warranties provide lifetime replacement and limited financial reimbursement in the event of loss of shell integrity resulting in implant deflation, subject to certain conditions as fully discussed in the ConfidencePlus™ literature. For more information, please contact Product Support at 800.624.4261.

Product Ordering

To order directly in the U.S.A or for product information, please contact your local INAMED Aesthetics Sales Representative or the INAMED Customer Care Department at 800.766.0171.

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