

© INAMED
PMA #P020056
Silicone-Filled Breast Implants

CONFIDENTIAL

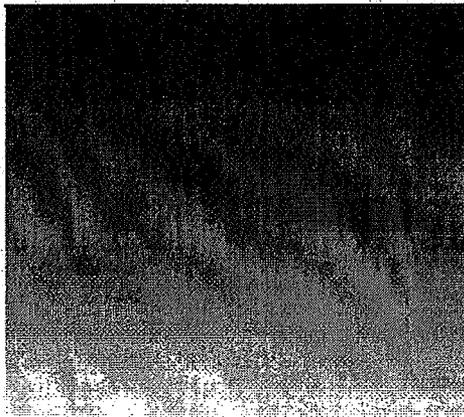
ATTACHMENT 9-1
PACKAGE INSERT (DFU)

002554

Directions for Use

BIOCELL[®] Textured and Smooth

SILICONE-FILLED
BREAST IMPLANTS



 **INAMED**
AESTHETICS

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

Table of Contents

SECTION	PAGE
Introduction	
Directions to the Surgeon	
Information to be Discussed with the Patient	
Device Description	
Indications	
Contraindications	
Warnings	
Precautions	
Special Considerations to be Discussed with the Patient	
Preclinical Study Information	
Clinical Studies	
Study Design	
Safety Outcomes	
Potential Adverse Events	
Effectiveness Outcomes	
Instructions for Use	
Single Use	
Product Identification	
Surgical Planning	
Preliminary Product Examination	
Sterile Product	
Surgical Procedure	
Documentation the Physician Should Provide to the Patient	
Specific Product Information	
BIOCELL® Delivery Assistance Sleeve	
Returned Goods Policy	
Reporting and Return of Explanted Devices	
ConfidencePlus™ Breast Implant Replacement Program	
Product Ordering	

INTRODUCTION

• **DIRECTIONS TO THE SURGEON**

This document contains information that is essential to the patient consultation process. Please familiarize yourself with the content of this document and resolve any questions or concerns prior to proceeding with use of the device.

The information supplied in this Direction for Use document is intended to provide an overview of the appropriate use of INAMED silicone-filled breast implants, contraindications for use, warnings, including surgical techniques that should be avoided as it may compromise implant integrity, precautions, adverse and potential adverse events, as well as a clinical study summary.

Patient Counseling Information

Sections of this *Directions for Use* document indicated by "***Patient Counseling Information***" contain points that the physician should review when counseling the patient about silicone-filled breast implants and breast implant surgery.

• **INFORMATION TO BE DISCUSSED WITH THE PATIENT**

WARNINGS, PRECAUTIONS, ADVERSE EVENTS

Patient Counseling Information

Breast implant surgery is known to provide satisfaction to patients, *HOWEVER*, as with any surgical procedure, it is *NOT* without risks. Breast implantation is an elective procedure, and the patient must be well counseled on the risk/benefit relationship.

Before the decision to proceed with surgery, the surgeon or a designated patient counselor should inform the patient of the warnings, precautions, and adverse reactions listed in this *Directions for Use* document. The physician should advise the patient that medical management of serious adverse reactions may include explantation.

INFORMED CONSENT

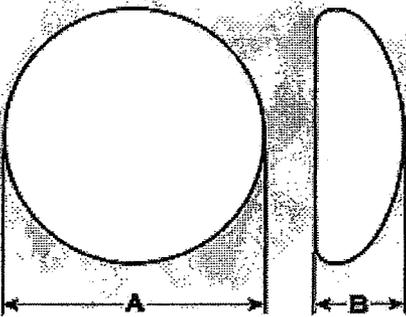
Patient Counseling Information

Each patient should read, understand, sign, and date the document ***Making an Informed Decision; Silicone Filled Breast Implant Surgery*** supplied by INAMED Corporation, which contains important information on the benefits and possible risks associated with silicone-filled breast implant surgery.

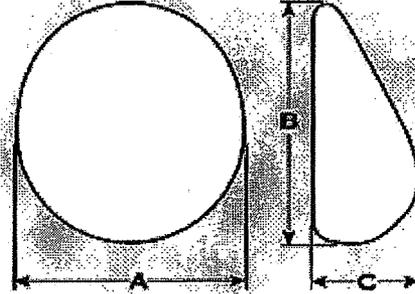
DEVICE DESCRIPTION

INAMED Aesthetics Silicone-Filled Breast Implants are constructed with barrier shell technology resulting in a low diffusion silicone elastomer shell and are filled with a soft, cohesive silicone gel. INAMED Aesthetics Silicone-Filled Breast Implants are available in both smooth and BIOCELL[®] surface textures in round and shaped designs.

Refer to the INAMED Aesthetics product catalog for a complete list of implant options and sizes.



**A = Width; B = Projection
Round Breast Implant**



**A = Width; B = Height; C = Projection
Shaped Breast Implant**

INDICATIONS

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

CONTRAINDICATIONS

Patient Groups in which the product is contraindicated:

- **Women with existing malignant or pre-malignant cancer of the breast without adequate treatment**
- **Women with an active infection anywhere in the body**
- **Women who are currently pregnant or nursing**
- **Augmentation in women under the age of 18 years**

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

- **Alteration:** Do not alter the implant.
- **Stacking of implants:** Do not place more than one implant per breast.
- **Reuse:** See "Instructions for Use" section.

WARNINGS

AVOID DAMAGE DURING SURGERY

- ***Care should be taken to avoid the use of excessive force and to minimize handling of the implant during surgical insertion.***

Based on analyses of explanted ruptured silicone-filled breast implants, observations of surgeries, and a review of the published literature, INAMED believes that the forcing of implants through small incisions may result in localized weakening of the breast implant shell potentially leading to shell damage and possible implant rupture.

- ***Care should be taken when using surgical instruments in proximity with the breast implant, including scalpel, sutures, and dissection instrumentation.***

Silicone-filled breast implants are prone to unintended instrument trauma during implantation or during explantation (Brandon et al. 2001, Young and Watson 2001). Failure can result from damage by scalpels, suture needles, hypodermic needles, hemostats, and Adson forceps and has been observed in explanted device shells using scanning electron microscopy (Brandon et al. 2001).

- ***Use care in subsequent procedures such as open capsulotomy, breast pocket revision, hematoma/seroma aspiration, and biopsy/lumpectomy to avoid damage to the implant.***

Re-positioning of the implant during subsequent procedures should be carefully evaluated by the medical team and care taken to avoid contamination of the implant before placement back in the pocket. Use of excessive force during removal and replacement can contribute to localized weakening of the breast implant shell potentially leading to decreased device performance.

- ***Do not contact the implant with disposable, capacitor-type cautery devices.***
- ***Do not insert or attempt to repair a damaged prosthesis.***

CLOSED CAPSULOTOMY

DO NOT treat capsular contracture by forceful external compression, which will likely result in implant damage, rupture, folds, and/or hematoma.

SINGLE USE DEVICES

Breast implants are single use devices only. Do not resterilize or reuse.

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

PRECAUTIONS

SPECIFIC POPULATIONS

Safety and Effectiveness have not been established in patients with:

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

MAMMOGRAPHY

Patient Counseling Information

Breast implants may complicate the interpretation of mammographic images by obscuring underlying breast tissue and/or by compressing overlying tissue. The ability of mammography to detect cancer or implant rupture in patients with breast implants has been evaluated in numerous studies. Standard compression mammography is insufficient by itself to detect many palpable tumors (Carlson et al. 1993), but the detection rate improves when combined with displacement techniques (Eklund et al. 1988). Accredited mammography centers and use of displacement techniques are needed to adequately visualize breast tissue in the implanted breast. Radiologists should be experienced with the most current radiological techniques and equipment for imaging breasts with implants.

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.

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.

LONG-TERM EFFECTS

Patient Counseling Information

Although clinical study follow-up data has been collected through 4 years, the long-term safety and effectiveness of INAMED's Silicone-Filled Breast Implants has not been established. INAMED is monitoring the long-term (i.e., 10-year) risk of implant rupture, reoperation, implant removal, breast disease and other local and systemic complications.

SPECIAL CONSIDERATIONS TO BE DISCUSSED WITH THE PATIENT

Patient Counseling Information

The following information should be discussed with patients prior to their decision to proceed with surgery:

- ***Professional Care*** – Patients should be advised that follow-up exams as prescribed by their plastic surgeon are recommended to monitor the status of their breast implants.
- ***Reoperation*** – Patients should be advised that additional surgery to their breast and/or implant may be necessary over the course of their life.
- ***Explantation*** – Patients should be advised that implants are not considered life-time devices, and they will potentially 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, type, and placement of their implants. Patients should be advised to request diagnostic mammography rather than screening mammography.
- ***Lactation*** – Patients should be advised that breast implants may interfere with the ability to successfully breast feed.
- ***Infection*** – In rare instances, acute infection may occur in a breast with implants. The signs of acute infection include erythema, tenderness, fluid accumulation, pain and fever. Very rarely, Toxic Shock Syndrome, a potentially life-threatening condition, has been reported in women after breast implant surgery. It is characterized by symptoms that occur suddenly and include high fever (102°F, 38.8°C or higher), vomiting, diarrhea, a sunburn-like rash, red eyes, dizziness, lightheadedness, muscle aches, and drops in blood pressure, which may cause fainting. Patients should be advised to contact a physician immediately for diagnosis and treatment for any of these symptoms.
- ***Avoiding Damage during Treatment*** – Patients should be instructed to inform other treating physicians of the presence of implants to minimize the risk of damage to the implants.
- ***Smoking*** – Patients should be informed that smoking may interfere with the healing process.

- ***Cosmetic Dissatisfaction*** – Patients should be informed that dissatisfaction with cosmetic results related to such things as scar deformity, hypertrophic scarring, capsular contracture, asymmetry, displacement, incorrect size, unanticipated contour, and palpability may occur. Careful surgical planning and technique can minimize, but not preclude, the risk of such results. Pre-existing asymmetry may not be entirely correctable. Physiological and behavioral differences among patients and variations in surgical techniques and medical treatments account for a wide variety of responses to silicone-filled breast implant surgery. Revision surgery may be indicated to maintain patient satisfaction but carries additional considerations and risks.
- ***Breast Examination Techniques*** – Patients should be instructed to follow the most current medical recommendations regarding breast examination and mammography frequency appropriate for their age and medical history. To maximize the effectiveness of breast self examinations for any palpable lesions, patients should be instructed how to distinguish the implant from breast tissue.
- ***Monitoring for Asymptomatic Implant Rupture*** – Patients should be informed that periodic evaluation of the integrity of their breast implants is required to determine whether the implant has ruptured in the absence of any clinical symptoms. While there are various diagnostic methods available to evaluate for possible implant rupture including physical examination, mammogram, and ultrasound, FDA believes the best method for detection of rupture is Magnetic Resonance Imaging (MRI). In most cases, an MRI diagnosis of rupture or possible rupture is consistent with a ruptured implant at explantation (Brown et al. 2000, Holmich et al. 2004). INAMED's clinical study results and other published reports have found that in some cases MRI may falsely show a breast implant rupture when there is none. Scaranelo et al. (2004) found that the sensitivity and specificity of MRI to detect rupture in asymptomatic patients was 64% and 77%, respectively. Thus, MRI findings of rupture should not be considered definitive (Scaranelo et al. 2004). MRI screening should be performed every 1-2 years or at a frequency recommended by the patient's plastic surgeon.
- ***Clinical Management of Suspected and Confirmed Rupture*** – Patients should be informed that following a diagnosis of suspected or confirmed rupture that implant removal might be recommended by the surgeon, particularly in those instances where there may be evidence that silicone gel has moved beyond the confines of the fibrous capsule that typically forms around the device. Most surgeons in INAMED's clinical studies have chosen to remove implants suspected of rupture. The decision to remove an asymptomatic but ruptured implant should be undertaken following discussion between the patient and the surgeon.

Patients should be aware that, rarely, an intracapsular rupture may progress to an extracapsular rupture. Holmich et al. (2004) conducted a study of whether ruptured breast implants are associated with changes over time according to MRI evaluations taken 2 years apart. They found that of 77 implants with MRI evidence of intracapsular rupture at baseline, MRI revealed that 7 (9%) had evidence of extracapsular silicone 2 years later. The decision to remove a ruptured implant with the presence of either intracapsular or extracapsular gel should be undertaken following review of all available clinical information and after careful consideration between the patient and the surgeon.

COMPLICATIONS

Patient Counseling Information

The following is a list of potential adverse events that may occur with breast implant surgery. Some of these adverse events are reported in Tables 1 and 6 below. The risks include: implant rupture, additional surgery, capsular contracture, infection, Toxic Shock Syndrome (TSS), 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), 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 has been discussion in the scientific and regulatory communities regarding the potential for silicone-filled breast implants to be associated with certain systemic diseases or concerns.

- **Systemic (CTD) Diseases**

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. Several large epidemiological studies of women with and without implants indicate that these diseases are no more common in women with implants than in those women without implants.

Some patients in INAMED's Core Clinical Study showed an increase over time in some CTD signs and symptoms and those CTD signs and symptoms specific to fibromyalgia, such as fatigue, swelling, weakness, aches, back and neck pain. However, patients with INAMED's saline-filled implants showed similar increases in these signs and symptoms. This indicates that the increased signs and symptoms are most likely not caused by the silicone-filled breast implants and may be attributed to other factors such as aging.

- **Suicide**

Some investigators have raised concerns that the risk of suicide is increased in patients with silicone-filled breast implants (Brinton et al. 2001, Koot et al. 2003, Pukkala et al. 2003, Jacobsen et al. 2003). The studies are not designed to account for very significant potential confounding factors that are likely to affect a woman's predisposition for suicidal tendencies and that are widely acknowledged to be more prevalent among women who seek breast implants (e.g., cigarette smoking, alcohol consumption, weight, parity, low self-esteem, depression, or other psychiatric/emotional disorders) (McLaughlin et al. 2003, McLaughlin et al. 2004).

- **Cancer**

Published clinical studies indicate that breast cancer is no more common in women with implants than those without implants (Institute of Medicine 2000, McLaughlin et al. 1994, Friis et al. 1997, Møller 2000). Furthermore, basic animal toxicological studies as discussed in INAMED's Summary of Safety & Effectiveness Data (SSED) document (www.tdb.gov) do not find pathology that would support a causation of human carcinogenicity by silicone breast implants.

- **Effects on Breast Milk**

At this time it is not known if a small amount of silicone may diffuse from the silicone-filled breast implant and find its way into breast milk. If this occurs, it is not known what effect it may have on the nursing infant. There have been some studies that reported evidence of esophageal dysmobility and gastrointestinal effects in breastfed children of women with implants, but there is insufficient evidence that this is a result of exposure to silicone. There is evidence that silicon concentrations in breast milk are the same in mothers with and without breast implants (Lugowski et al. 1998). The American Academy of Pediatrics prepared a statement on the transfer of drugs and other chemicals into human milk in September 2001, which concluded "The Committee on Drugs does not feel that the evidence currently justifies classifying silicone implants as a contraindication to breastfeeding."

- **Second-Generation Effects**

The concern that children born to mothers with silicone breast implants are at risk of developing adverse health outcomes stems from reports of children born to or breastfed by such women who developed swallowing difficulties, irritability, nonspecific skin rashes, fatigue, and other symptoms (Levine and Ilowite 1994, Levine et al. 1996). However, epidemiological investigations have not found any increased risk of adverse health outcomes, including occurrence of esophageal disorders, connective tissue disease, and congenital malformations in children born to women with breast implants (Kjoller et al. 1998, Kjoller et al. 2002, Signorello et al. 2001).

- **Potential systemic health consequences of extracapsular or migrated gel following rupture**

When breast implants rupture, in most cases, any silicone gel that is released from the device is contained in the fibrous capsule that develops around the device shortly after implantation. If there is a loss of integrity in the fibrous capsule, which most likely occurs as a result of closed capsulotomy, trauma, or compression mammography, silicone gel may migrate from the implant through the capsule and into the surrounding breast tissue. The medical literature suggests that approximately 25% of ruptured breast implants may have evidence of silicone gel in the breast tissue around the fibrous capsule (Holmich et al. 2001, Berg et al. 2002, Herborn et al. 2002, Holmich et al. 2003). There has been no clinical evaluation of the migration of silicone gel from a ruptured implant beyond breast tissue, but the medical literature contains a relatively small number of case reports of silicone gel detected distant from the implantation, primarily in women with ruptured implants. The frequency of this event is quite rare given the millions of breast implants that have been implanted.

Extracapsular gel or migration of gel may be accompanied by localized pain or discomfort. Holmich et al. (2004) conducted MRI analysis of 64 Danish women (126 implants) who were found to have a ruptured implant in an earlier study (96/126 ruptured implants), where the implants were not removed. The authors obtained questionnaire data on symptoms that developed between the first and second MRI examinations. The results were compared to all women with intact implants at both MRI assessments (98 women with 193 intact implants) for self-reported breast symptoms. Compared to women with intact implants, women with ruptured implants reported a significantly increased frequency of non-specific breast changes, changes in breast shape, breast pain, and any breast change. There is no evidence that extracapsular gel or migrated gel pose risk of systemic disease in breast implant patients.

- **Local complications potentially associated with gel diffusion (bleed)**

There is no evidence from the medical literature or from Inamed's own testing suggesting that gel bleed (diffusion) may be associated with local complications in breast implant patients. In addition, clinical study patients in Inamed's Core clinical study for silicone-filled breast implants were at no higher risk of local complications when compared to the risk of local complications reported in Inamed's 1995 saline-filled breast implant clinical study. INAMED conducted *in-vitro* testing in order to mimic a lipid-rich *in-vivo* environment to determine bleed rate over time, and to identify the constituents of gel diffusion (bleed). There was no evidence that the catalysts, platinum or tin, are contained in the constituents of silicone gel bleed under the conditions of the test method.

002567

PreCLINICAL STUDY INFORMATION

Preclinical study of INAMED's Silicone-Filled Breast implants revealed that the materials of which the device is made are biocompatible, the silicone elastomer shell is durable, and there is a low potential for filler bleed. A summary of preclinical studies conducted including chemistry, toxicology, and physical/mechanical testing can be found in the SSED document on the FDA website at www.tdb.gov.

CLINICAL STUDIES

CORE CLINICAL STUDY

Study Design

The safety and effectiveness of INAMED Silicone-Filled Breast Implants were evaluated in three open-label, multicenter clinical studies: the 1990 Augmentation/Reconstruction Study (AR90), the Core Study and the Adjunct Study. Because the 1990 Study utilized devices and surgical practices that are no longer current, these data are not reported below.

The Core Study was designed as a 10-year study to assess safety and effectiveness. Patients studied were those seeking implant surgery for breast augmentation, breast reconstruction, or revision of an existing breast implant. Follow-up was at 0-4 weeks, 6 months, and annually through 10 years, and is currently ongoing. Safety assessments consisted of adverse event rates and rates of secondary surgical treatment. Effectiveness assessments consist of patient satisfaction, breast size change, and measures of body esteem/self esteem/body image.

Patient Accounting and Baseline Demographic Profile

The Core Study enrolled 494 augmentation patients, 221 reconstruction patients, and 225 revision patients. Of those patients expected to be seen, 86% of the augmentation patients, 94% of the reconstruction patients, and 87% of the revision patients were seen for their 3-year follow-up visit. *[Note that 3-year data are the most current data available.]*

Demographic information obtained from the Core Study revealed that over 80% of patients were Caucasian and most study participants were married (49% of augmentation patients, 75% of reconstruction patients, and 64% of revision patients). Approximately half were employed in professional occupations and more than three fourths had at least some college education. The median patient age was 34 years for augmentation patients, 50 years for reconstruction patients, and 44 years for revision patients. *[Note that 3-year data are the most current data available.]*

With respect to surgical baseline factors in the Core Study, for augmentation patients, the most frequently used devices were round, with a smooth surface somewhat more common than textured. The most common incision sites were inframammary and periareolar, and the most frequent placement of the implant was submuscular. For reconstruction patients, the most frequently used devices were shaped with a textured surface, the most common incision site was the mastectomy scar, and the most frequent placement of the implant was submuscular. For revision patients, the most frequently used devices were round, and the textured surface (round and shaped) was more common than smooth. The most common incision site was inframammary, and the most frequent placement of the implant was submuscular.

SAFETY OUTCOMES

Adverse Events

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 **Table 1** based on indication.

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

Complication*	Augmentation N = 494		Reconstruction N = 221		Revision N = 225	
	Rate (%)	(95% CI)	Rate (%)	(95% CI)	Rate (%)	(95% CI)
Reoperation*	21.1	(17.4, 24.7)	47.2	(40.5, 53.9)	35.1	(28.7, 41.6)
Capsular Contracture	9.7	(7.0, 12.3)	15.1	(10.1, 20.0)	14.1	(9.4, 18.9)
Implant Replacement/Removal*	7.0	(4.7, 9.3)	21.6	(16.0, 27.1)	12.9	(8.3, 17.4)
Breast Pain	6.9	(4.6, 9.2)	5.9	(2.6, 9.1)	6.6	(3.2, 9.9)
Swelling	6.7	(4.5, 9.0)	4.6	(1.8, 7.3)	5.5	(2.5, 8.6)
Loss of Nipple Sensation	3.5	(1.9, 5.2)	0	—	0	—
Asymmetry	3.0	(1.4, 4.5)	13.4	(8.7, 18.0)	4.5	(1.6, 7.4)
Implant Malposition	2.9	(1.4, 4.4)	7.5	(4.0, 11.0)	4.8	(1.9, 7.7)
Hypertrophic/Abnormal Scarring	2.7	(1.3, 4.2)	3.9	(1.2, 6.5)	4.5	(1.6, 7.3)
Ptosis	1.9	(0.7, 3.1)	<1	<1	<1	<1
Seroma/Fluid Accumulation	1.2	(0.3, 2.2)	1.8	(0.1, 3.6)	5.2	(2.2, 8.2)
Skin Rash	1.2	(0.3, 2.2)	1.4	(0.0, 2.9)	1.0	(0.0, 2.3)
Hematoma	1.2	(0.3, 2.2)	<1	<1	1.4	(0.0, 2.9)
Nipple Hypersensitivity/Paresthesia	1.2	(0.3, 2.2)	<1	<1	0	—
Implant Palpability/Visibility	1.1	(0.1, 2.0)	<1	<1	2.9	(0.6, 5.1)
Loss of Skin Sensation	1.1	(0.1, 2.0)	0	—	<1	<1
Implant Rupture	2.0	(0.4, 1.7)	11.0	(4.1, 9.8)	5.0	(1.0, 4.3)
Bruising	<1	<1	1.4	(0.0, 2.9)	1.8	(0.1, 3.5)
Tissue or Skin Necrosis	<1	<1	3.8	(1.2, 6.3)	1.4	(0.0, 3.0)
Wrinkling/Rippling	<1	<1	3.4	(0.9, 5.9)	5.4	(2.3, 8.6)
Redness	<1	<1	2.0	(0.1, 3.8)	<1	<1
Delayed Wound Healing	<1	<1	1.8	(0.1, 3.6)	<1	<1
Infection	<1	<1	1.9	(0.1, 3.7)	1.8	(0.1, 3.6)

* All complications other than reoperation and implant replacement/removal were assessed with severity ratings. Most rates shown in the table include only complications rated moderate, severe or very severe (excludes mild and very mild ratings). The only complication rates that include all severity ratings are rupture, pneumothorax and implant extrusion.

Reoperation

Of the 494 augmentation patients in the Core Study, at least one additional operation after the initial implantation (reoperation) was performed on 101 patients (20.4%) through 3 years. A total of 123 reoperations were performed on augmentation patients over 3 years.

Of the 221 reconstruction patients in the Core Study, at least one reoperation was performed on 102 patients (46.2%) through 3 years. A total of 144 reoperations were performed on reconstruction patients over 3 years, excluding planned procedures such as nipple reconstruction and nipple tattoo.

Of the 225 revision patients in the Core Study, at least one reoperation was performed on 75 patients (33.3%) through 3 years. A total of 115 reoperations were performed on revision patients over 3 years.

Table 2 shows the types of reoperations performed through 3 years in the Core Study based on the total number of reoperations.

Table 2
Types of Reoperations through 3 Years

Type of Reoperation ¹	Augmentation N = 123 Reoperations		Reconstruction N = 144 Reoperations		Revision N = 115 Reoperations	
	n	percent	n	percent	n	percent
Implant Replacement/Removal ²	33	27	47	34	29	25
Capsule Procedure ³	29	24	21	15	24	21
Scar Revision	14	11	25	17	13	11
Mastopexy	14	11	3	2	9	8
Biopsy	11	9	5	4	5	4
Aspiration of Hematoma/Seroma	9	7	9	6	10	9
Reposition Implant	4	3	6	4	2	2
Wound Repair	3	2	9	6	4	4
Pocket Revision	3	2	4	3	6	5
Revision of Nipple Reconstruction/Tattoo	1	1	6	4	8	7
Removal of Excess Tissue/Lesion/Cyst	1	1	2	1	2	2
Surgical Exploration of Breast Area/Implant	1	1	1	1	1	1
Liposuction	0	0	5	4	1	1
Breast Reduction	0	0	1	1	1	1
Total	123	100	144	100	115	100

¹Primary procedure performed

²Some removals were replaced with an INAMED implant, while others were replaced with a non-INAMED implant

³Capsule Procedure includes capsulectomy, capsulotomy, and capsulorrhaphy

Implant Removal

Of the 494 augmentation patients in the Core Study, there were 33 patients (6.7%) who had 62 implants removed through 3 years. Of the 62 augmentation implants removed through 3 years, 82% were replaced.

Of the 221 reconstruction patients in the Core Study, there were 46 patients (20.8%) who had 56 implants removed through 3 years. Of the 56 reconstruction implants removed through 3 years, 91% were replaced.

Of the 225 revision patients in the Core Study, there were 27 patients (12.0%) who had 46 implants removed through 3 years. Of the 46 revision implants removed through 3 years, 89% were replaced.

The primary reason for implant removal is shown in **Table 3** below based on the number of implants removed.

Table 3
Reasons for Implant Removal Through 3 Years

Primary Reason for Implant Removal	Augmentation N = 62 Implants		Reconstruction N = 56 Implants		Revision N = 46 Implants	
	n	percent	n	percent	n	percent
Capsular Contracture	25	40	11	20	8	17
Style/Size Change (Patient Request)	11	18	4	7	11	24
Silicone Anxiety (Patient Request)	7	11	0	0	0	0
Asymmetry	4	6	11	20	1	2
Malposition	4	6	10	18	8	17
Ptosis	4	6	0	0	4	9
Implant Rupture	2	3	7	13	6	13
Nipple Complications	2	3	1	2	0	0
Hematoma/Seroma	1	2	3	5	0	0
Breast Cancer	1	2	1	2	0	0
Extrusion	1	2	1	2	0	0
Wrinkling	0	0	3	5	0	0
Pain	0	0	2	4	1	2
Breast Tissue Contour Deformity	0	0	1	2	2	4
Injury (Iatrogenic or Traumatic)	0	0	1	2	0	0
Infection	0	0	0	0	2	4
Unsatisfactory Scar	0	0	0	0	2	4
Delayed Wound Healing	0	0	0	0	1	2
Total	62	100	56	100	46	100

CTD and Breast Disease

Tables 4 and 5 summarize post-implant observations from the Core Study pertaining to connective tissue/autoimmune disease (CTD) 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. CTD reports were based on a diagnosis by a physician.

Table 4
Reports of CTD through 3 Years, By Patient

Rheumatic Disease	No. of Confirmed Reports in Patients		
	Augmentation	Reconstruction	Revision
Rheumatoid Arthritis	2	0	0
Systemic Sclerosis/Scleroderma	0	1	0
Fibromyalgia	0	0	1

Table 5
Risk of Breast Disease through 3 Years, By Patient

Breast Disease Observation	Rate (%) of Confirmed Reports in Patients		
	Augmentation	Reconstruction	Revision
Benign	6.4	5.1	9.0
Malignant	<1	5.2	0
Unknown Outcome	1.8	2.1	1.0

Effectiveness Outcomes

Core Study

Effectiveness of silicone-filled breast implants was assessed in the Core Study 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 silicone devices before implantation and at 2 years after surgery, except for bra size which was measured within the first year and a half after surgery and based only on original silicone devices. Satisfaction was measured at every follow-up visit through 3 years.

Augmentation

408 of the original 494 augmentation patients (83%) at 18 months were included in an analysis of cup size (17% did not provide data because pre/post measurements were not obtained or replacement/removal occurred prior to obtaining a post measurement). Of these 408 patients, the following shows the percentage of patients experiencing various changes in cup size:

- Increase by 1 cup size: 41%
- Increase by 2 cup sizes: 45%
- Increase by more than 2 cup sizes: 8%
- No Increase: 6%

410 of the original 494 augmentation patients (83%) were included in an analysis of satisfaction at 3 years. Of these 410 patients, 96% indicated being satisfied with their breast implants at 3 years. Furthermore, augmentation patients showed a statistically significant increase in satisfaction with breast size and shape after implantation.

The Quality-of-Life patient surveys showed that augmentation patients scored higher (better) than the general U.S. female population on the SF-36 scales, which measure general health-related quality of life. However, after 2 years, patients showed a slight worsening in their SF-36 scores possibly due to the increase in patient age or other lifestyle changes. Although they did worsen, they continued to remain higher than the U.S. female population. The following two scales showed no change over the 2 years: The Tennessee Self Concept Scale (which measures overall self concept) and The Rosenberg Self Esteem Scale (which measures overall self esteem). The Body Esteem Scale (which measures overall self esteem related specifically to one's body) showed a slight improvement over the 2 years. The scales described above have been validated and are widely used in various research fields. All scales contain multiple questions that are answered by the patient on the Quality-of-Life patient surveys obtained during the course of the study; a composite score for each scale is created using the responses to each of the individual questions in each scale. The

conclusions drawn above are the result of comparing each patient's baseline composite score to her corresponding 2-year composite score.

Reconstruction

185 of the original 221 reconstruction patients (84%) were included in an analysis of satisfaction at 3 years. Of these 185 patients, 92% indicated being satisfied with their breast implants at 3 years. Reconstruction patients also showed a statistically significant increase in satisfaction with breast size and shape after implantation.

The Quality-of Life patient surveys showed that reconstruction patients scored higher (better) than the general U.S. female population on the SF-36 scales, which measure general health-related quality of life. After 2 years, patients showed no change from baseline in most of the general health-related attributed measured by the SF-36 indicating that their general health related quality of life remained higher than the U.S. female population. The following two scales showed no change over the 2 years: The Tennessee Self Concept Scale (which measures overall self concept) and The Rosenberg Self Esteem Scale (which measures overall self esteem). Furthermore, The Body Esteem Scale (which measures overall self esteem related specifically to one's body) showed a no change over the 2 years post-implantation. The scales described above have been validated and are widely used in various research fields. All scales contain multiple questions that are answered by the patient on the Quality-of-Life patient surveys obtained during the course of the study; a composite score for each scale is created using the responses to each of the individual questions in each scale. The conclusions drawn above are the result of comparing each patient's baseline composite score to her corresponding 2-year composite score.

Revision

183 of the original 225 revision patients (81%) were included in an analysis of satisfaction at 3 years. Of these 183 patients, 88% indicated being satisfied with their breast implants at 3 years. Revision patients also showed a statistically significant increase in satisfaction with breast size and shape after implantation.

The Quality-of Life patient surveys showed that revision patients scored higher (better) than the general U.S. female population on many of the SF-36 scales, which measure general health-related quality of life. However, after 2 years, patients showed a slight worsening in their SF-36 scores possibly due to the increase in patient age or other lifestyle changes. Although they did worsen, they continued to remain higher than the U.S. female population. The following two scales showed a decrease (worsening) over the 2 years: The Tennessee Self Concept Scale (which measures overall self concept) and The Rosenberg Self Esteem Scale (which measures overall self esteem). However, The Body Esteem Scale (which measures overall self esteem related specifically to one's body) showed a no change over the 2 years post-implantation; this scale may be more informative in measuring the impact of breast implants because it is specific to the patient's body. The scales described above have been validated and are widely used in various research fields. All scales contain

002576

multiple questions that are answered by the patient on the Quality-of-Life patient surveys obtained during the course of the study; a composite score for each scale is created using the responses to each of the individual questions in each scale. The conclusions drawn above are the result of comparing each patient's baseline composite score to her corresponding 2-year composite score.

ADJUNCT STUDY

Study Design

The Adjunct Study was designed as a prospective 5-year study to assess safety outcomes for a large number of patients. Patients studied were those seeking breast reconstruction or revision of an existing implant for medical reasons. Follow-up was at 1, 3, and 5 years and is currently ongoing. Safety assessments consisted of adverse event rates and rates of secondary surgical treatment.

Patient Accounting and Baseline Demographic Profile

The Adjunct Study enrolled 22,884 reconstruction patients and 23,575 revision patients over 6 years. Of those reconstruction patients expected to be seen, 9,198 (55.6%) returned for their 1-year follow-up visit and 2,552 (34.8%) returned for their 3-year follow-up visit. Of those revision patients expected to be seen, 9,006 (49.0%) returned for their 1-year follow-up visit and 2,833 (29.1%) returned for their 3-year follow-up visit.

Demographic information obtained from the Adjunct Study revealed that approximately 60% of participants were married, more than 40% were employed in professional occupations, and more than 70% had at least some college education. The median patient age was 42 years for reconstruction patients and 46 years for revision patients.

With respect to surgical baseline factors in the Adjunct Study, for both reconstruction and revision patients, the most frequently used devices were round with a fairly equal distribution of smooth and textured surface.

Safety Outcomes

Adverse Events

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 **Table 6** based on indication.

Table 6
3-Year Cumulative First Occurrence Kaplan-Meier
Adverse Event Risk Rates (95% Confidence Interval), By Patient

Complication	Reconstruction N = 22,884		Revision N = 23,575	
	Rate (%)	(95% CI)	Rate (%)	(95% CI)
Reoperation*	38.6	(37.4, 39.8)	29.5	(28.4, 30.5)
Implant Replacement/Removal*	23.2	(22.1, 24.3)	19.9	(18.9, 20.9)
Capsular Contracture	12.2	(11.2, 13.1)	14.8	(13.9, 15.8)
Asymmetry	10.2	(9.3, 11.0)	8.7	(7.9, 9.4)
Wrinkling	5.8	(5.1, 6.5)	8.9	(8.2, 9.7)
Implant Malposition	5.6	(5.0, 6.3)	5.6	(5.0, 6.3)
Implant Palpability/Visibility	5.5	(4.8, 6.1)	8.6	(7.9, 9.4)
Breast Pain	4.5	(3.9, 5.1)	6.0	(5.3, 6.6)
Loss of Nipple Sensation	3.5	(3.0, 4.0)	3.1	(2.6, 3.6)
Hypertrophic Scarring	2.0	(1.6, 2.4)	1.9	(1.5, 2.2)
Capsule Calcification	1.7	(1.3, 2.1)	2.3	(1.9, 2.7)
Skin Hypersensitivity/Paresthesia	1.6	(1.3, 2.0)	1.6	(1.3, 2.0)
Swelling	1.4	(1.1, 1.7)	1.6	(1.3, 1.9)
Nipple Hypersensitivity/Paresthesia	1.1	(0.8, 1.4)	1.0	(0.7, 1.3)
Implant Rupture*	<1	<1	<1	<1

*All complications other than reoperation and implant replacement/removal were assessed with severity ratings. Most rates shown in the table include only complications rated moderate, severe or very severe (excludes mild and very mild ratings). The only complication rates that include all severity ratings are rupture, pneumothorax and implant extrusion.

Effectiveness Outcomes

Effectiveness of silicone-filled breast implants was assessed in the Adjunct Study by patient reports of satisfaction at 1 and 3 years post-implant. Because this study continued to enroll patients over a 6-year period, many of the enrolled patients have not yet reached their 3-year follow-up visit. Thus, satisfaction data was available from a much smaller number of patients at 3 years than at 1 year.

For reconstruction patients, 9,090 of the original 22,884 patients (40%) were included in an analysis of satisfaction at 1 year post-implant; 60% were not included because these patients had not yet reached the 1-year follow-up time point, satisfaction data was not obtained at the 1-year visit, or implant replacement/removal occurred prior to 1 year). Of these 9,090 reconstruction patients, 93% indicated being satisfied with

their breast implants at 1 year. Satisfaction data was obtained from 2,599 reconstruction patients at 3 years post-implant. 94% of these patients indicated they were satisfied with their breast implants at 3 years.

For revision patients, 8,808 of the original 23,575 patients (37%) were included in an analysis of satisfaction at 1 year post-implant. Of these 8,808 revision patients, 91% indicated being satisfied with their breast implants at 1 year. Satisfaction data were obtained from 2,828 revision patients at 3 years post-implant. 91% of these patients indicated they were satisfied with their breast implants at 3 years.

INSTRUCTIONS FOR USE

NOTE: Back-up breast implants should 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 identification stickers accompany each device within the internal product packaging. The stickers provide product-specific information and are designed to be attached to the patient's chart for identification purposes.

Surgical Planning

INAMED relies on the surgeon to know and follow the proper surgical procedures with INAMED Silicone-Filled Breast Implants. 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 breast 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. The surgeon should observe current and accepted techniques to minimize the risk of adverse, and potentially disfiguring, reactions.

Preliminary Product Examination

How to Open Sterile Product Package

Remove the sterile breast implant from its package in an aseptic environment and using talc-free gloved hands. **DO NOT** expose the breast implant to lint, talc, sponge, towel, or other contaminants.

1. Peel open the lid of the outer thermoform package.
2. Invert the outer thermoform package over the sterile field, allowing the sealed inner thermoform package to gently fall into the field.

3. Peel open the lid of the inner thermoform package using the pull-tab.
4. Gently retrieve the breast implant. Prior to use, keep the breast implant in the inner thermoform package to prevent contact with airborne and surgical field particulate contaminants.

Examination of Silicone-Filled Breast Implants

Prior to use, examine the breast implant for evidence of any particulate contamination, damage, or loss of shell integrity. If satisfactory, return the breast implant to the inner thermoform tray and cover it with the lid until implanted to prevent contact with airborne contaminants.

DO NOT implant any device that may appear to have particulate contamination, damage, or loss of shell integrity. A sterile back-up implant must be readily available at the time of surgery.

DO NOT implant any device that may appear to have leaks or nicks.

DO NOT implant damaged or contaminated breast implants.

Sterile Product

Each sterile silicone-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 resterilize the product.

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.

Method for Removing Ruptured Silicone from the Surgical Pocket

In the event of breast implant rupture, the following technique is useful for removal of the silicone mass. Wearing double talc-free surgical gloves on one hand, use the index finger to penetrate the silicone mass. With the other hand, exert pressure on the breast to facilitate manipulation of the silicone mass into the double-gloved hand. Once the silicone is in hand, pull the outer glove over the silicone mass and remove. To remove any residual silicone, blot the surgical pocket with gauze sponges. Avoid contact between surgical instruments and the silicone. If contact occurs, use isopropyl alcohol to remove the silicone from the instruments. Ruptured breast implants must be reported and should be returned to INAMED. In the event of breast implant rupture, contact INAMED Product Support Department at 800.624.4261.

Surgical Procedure Placement

Ensure incision is sufficiently large to facilitate insertion without excessive manipulation and handling of the device and to avoid damage to the device. Inadequate pocket dissection increases the risk of rupture and implant malposition.

A sterile BIOCELL® Delivery Assistance Sleeve is available separately and can be used to assist with placement of the breast implant. Use of this sleeve for insertion of BIOCELL® textured breast implants provides a shell/tissue interface with less friction. Insert the 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 breast implant is inserted, gently remove the sleeve.

DO NOT use lubricants to facilitate placement. Their use creates the risk of pocket contamination and may also affect the tissue-capsule interface.

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

DO NOT use excessive force during breast implant placement.

DO NOT manipulate the implant for either radial expansion, compression or dissection of the pocket.

Breast augmentation with silicone-filled implants can be carried out through several different incisions including inframammary, periareolar, or transaxillary. 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. It is important to maintain proper orientation of any shaped 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 are 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 INAMED Aesthetics breast implants.

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.

DOCUMENTATION THE 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: Silicone-Filled Breast Implant Surgery***
This brochure should be used to facilitate patient education in the risks and benefits of silicone-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 silicone-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.
- ***Medical Device Registration***
INAMED Corporation maintains a device registry to identify patients who have INAMED's silicone-filled breast implants. The registry is designed to collect demographic and contact information for patients who are implanted with INAMED's silicone-filled breast implants. Information collected in the device registry may be provided, with patient consent, to research institutions engaged in large scale epidemiological studies.

INAMED strongly suggests that all patients receiving silicone-filled breast implants be registered in this database.

Successful device registration begins with the **Medical Device Registration Form** that is supplied with every breast implant. Stickers with product-specific

information are provided for quick completion of the form and are located on the internal product packaging attached to the label. If stickers are unavailable, the lot number, catalog number and description of each device may be copied by hand from the device label. The surgeon, medical facility or health care staff should fill out the top portion of the Medical Device Registration Form and then supply the entire form, along with the Device ID Card, to the patient. The patient should then complete the **Medical Device Registration Form** and return it to INAMED Corporation in the postage paid envelope provided.

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 an 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 or rupture, 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, the INAMED logo, BIOCELL, BioDIMENSIONAL, BIOSPAN, ZYDERM and ZYPLAST, ConfidencePlus are registered trademarks and/or trademarks of INAMED Corporation.

These products are covered by one or more of the following U.S. Patents: 5,480,430; 5,007,929; 4,889,744 and 4,859,712 and/or foreign patents corresponding thereto.



www.inamed.com

5540 Ekwill Street
Santa Barbara, CA 93111
800.624.4261
©2004 INAMED Corporation

M560 (*Draft 18August-04*)
www.InamedAesthetics.com