Bimini Health Tech

Puregraft Serene™ Breast Implant

Instructions for Use

WARNING

- **Breast implants are not considered lifetime devices. The longer patients have them, the greater the chances are that they will develop complications, some of which will require more surgery.**
- **Breast implants have been associated with the development of a cancer of the immune system called breast implant-associated anaplastic large cell lymphoma (BIA-ALCL). This cancer occurs more commonly in patients with textured-surface breast implants than smooth implants, although rates are not well defined. Some patients have died from BIA-ALCL.**
- **Patients receiving breast implants have reported a variety of systemic symptoms such as joint pain, muscle aches, confusion, chronic fatigue, autoimmune diseases and others. Individual patient risk for developing these symptoms has not been well established. Some patients report complete resolution of symptoms when the implants are removed without replacement.**

Caution: Federal law restricts this device to sale by or on the order of a licensed healthcare practitioner.

The sale and distribution of this device is restricted to users and/or user facilities that provide information to patients about the risks and benefits of this device in the form and manner specified in the FDA-approved labeling provided by Bimini Health Tech.

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DIRECTIONS TO THE PHYSICIAN

This document contains information that is essential to counseling the patient about Puregraft Serene Breast Implants and breast implant surgery. Please familiarize yourself with the content of this document and resolve any questions or concerns prior to proceeding with use of the device. The Puregraft Serene Breast Implant was previously marketed under the Ideal Implant tradename.

The information supplied in this Instructions for Use document is intended to provide an overview of essential information about Puregraft Serene Breast Implants, including the indications for use, contraindications, warnings, precautions, complications and a summary of Bimini Health Tech's clinical results.

Sections of this Instructions for Use document indicated by "**Patient Counseling Information"** contain points that the physician should review when counseling the patient about breast implants and breast implant surgery (also see Important Factors to be Discussed with the Patient on page 8).

INFORMATION TO BE DISCUSSED WITH THE PATIENT

WARNINGS, PRECAUTIONS, ADVERSE EVENTS

Patient Counseling Information
Breast implant surgery is known to provide satisfaction to patient, however, as with any surgical procedure, it is NOT without risks. Breast implantation is an elective procedure, and the patient must be well counseled and understand the risk/benefit relationship.

There is a boxed warning for all breast implants (See Cover Page 1)

Each patient should receive Bimini Health Tech's Patient Information Booklet, ***Making an Informed Decision Puregraft Serene Breast Implant Surgery,*** during her initial visit/consultation. The surgeon or a designated patient counselor should instruct the patient to read the patient information carefully and also discuss with the patient the warnings, precautions, and complications listed in this Instructions for Use document. The physician should advise the patient of the potential complications and that medical management of serious complications may include additional surgery and explantation.

Patients should understand that breast implant surgery can cause irreversible changes to the breast. A Patient Decision Checklist is included at the end of the Patient Information Booklet highlighting key information regarding risks. To help ensure that the material is read, reviewed, discussed and understood, the patient and physician should initial and/or sign the Checklist where indicated and receive a copy for future reference to this information.

INFORMED CONSENT

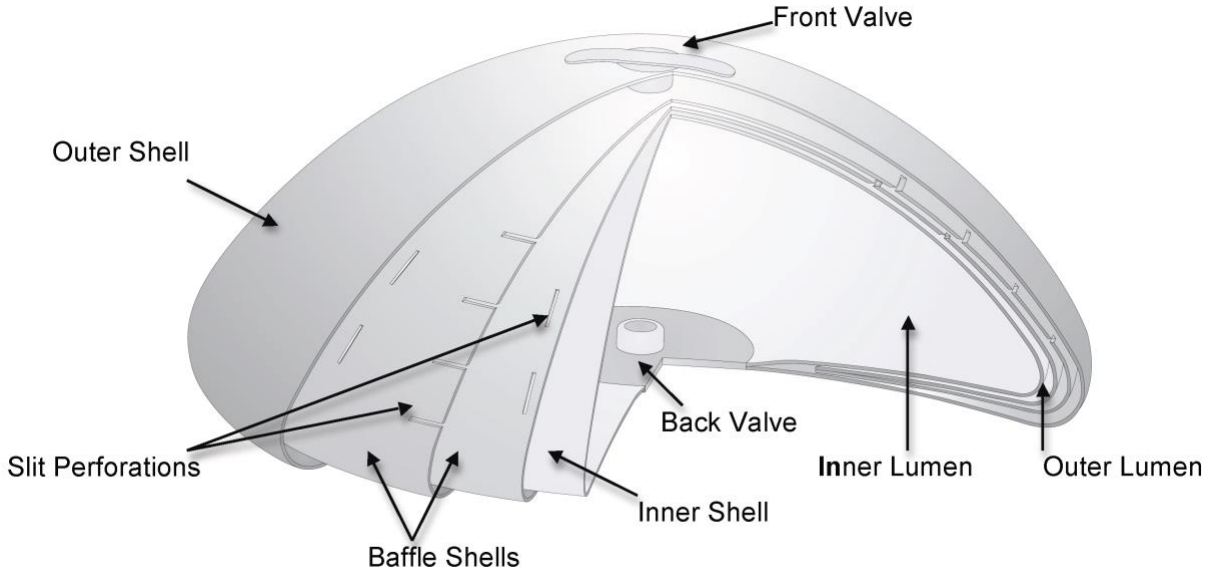
Patient Counseling Information
Before making the decision to proceed with surgery, the patient should be allowed at least 1-2 weeks to review and consider the information on the risks, follow-up recommendations, and benefits associated with saline-filled breast implant surgery. In the case of revision augmentation, it may be medically advisable to perform surgery sooner.

DEVICE DESCRIPTION

The Puregraft Serene Breast Implant is a round, smooth-surface, saline-filled breast implant with an internal structure that is supplied sterile in a dual tray packaging system with two disposable fill tubes and reflux valves. It was developed to provide women and surgeons with an alternative to saline-filled implants without an internal structure or silicone gel-filled implants.

FDA-approved saline-filled implants without an internal structure have a single lumen within a single shell made from cross-linked silicone elastomer. The Puregraft Serene Breast Implant has two lumens within two nested shells that are attached at the patch on the back of the implant. The inner lumen within the inner shell is filled through a valve in the patch. The outer lumen within the outer shell and surrounding the inner shell is filled through a valve on the front. Unattached and floating within the outer lumen is a baffle structure designed to restrict movement of the saline in the outer lumen. The amount of material required for the baffle structure is proportionate to the size of the implant and the fill volume in the outer lumen (Tables 1 and 2). This internal structure is comprised of one to three nested baffle shells that are perforated with slits so the saline is free to move through the slits, as well as around and between the shells. The inner and outer lumens are filled with saline before or after the implant has been placed in a submuscular or subglandular pocket. The materials, chemicals and heavy metals in this implant are listed in the Patient Information Booklet.

A cut-away drawing of a Puregraft Serene Breast Implant (335 cc to 555 cc size) shows the inner shell, the outer shell, the baffle structure floating in the outer lumen comprised of two baffle shells perforated with slits, the valve in the patch to fill the inner lumen and the valve on the front to fill the outer lumen.



Cut-away of Puregraft Serene Breast Implant (335 cc to 555 cc size) to show internal structure

Table 1 - Amount of Baffle Material (Shells) Relative to Implant Size and Outer Lumen Fill Volume		
Implant Size	**Outer Lumen Fill at Min.**	**Baffle Shells**
210 cc	60 cc	1
240 cc	65 cc	1
270 cc	70 cc	1
300 cc	75 cc	1
335 cc	95 cc	2
370 cc	100 cc	2
405 cc	110 cc	2
440 cc	115 cc	2
475 cc	120 cc	2
515 cc	125 cc	2
555 cc	135 cc	2
595 cc	155 cc	3
635 cc	160 cc	3
675 cc	160 cc	3

Table 2 - Approximate Dimensions and Volumes						
Size	Empty + Inner + Outer = Total Volume				Diameter	Projection
	Empty Implant Volume	Inner Lumen Saline	Outer Lumen Saline	Total Implant Volume		
			Min. – Max.	Min. – Max.	Min. – Max.	Min. – Max.
210 cc	30cc	120cc	60 - 85cc	210 - 235cc	10.1 – 10.0cm	3.5 - 4.3cm
240 cc	33	142	65 - 95	240 - 270	10.5 - 10.4	3.6 - 4.5
270 cc	35	165	70 - 105	270 - 305	11.0 - 10.8	3.8 - 4.7
300 cc	37	188	75 - 115	300 - 340	11.4 – 11.2	3.9 – 4.9
335 cc	52	188	95 - 135	335 - 375	11.9 - 11.7	4.0 - 5.1
370 cc	56	214	100 - 145	370 - 415	12.2 – 12.0	4.1 - 5.2
405 cc	60	235	110 - 160	405 - 455	12.5 – 12.4	4.2 - 5.4
440 cc	64	261	115 - 170	440 - 495	12.9 - 12.8	4.3 - 5.6
475 cc	68	287	120 - 180	475 - 535	13.3 – 13.1	4.4 - 5.7
515 cc	72	318	125 - 190	515 - 580	13.6 - 13.4	4.5 - 5.8
555 cc	76	344	135 - 205	555- 625	13.9 - 13.8	4.6 - 6.0
595 cc	94	346	155 - 230	595 - 670	14.3 – 14.2	4.7 - 6.1
635 cc	102	373	160 - 235	635 - 710	14.6 – 14.5	4.8 - 6.2
675 cc	110	405	160 - 240	675 - 755	14.9 - 14.8	4.9 - 6.3
Measured on a flat surface						

INDICATIONS

The Puregraft Serene Breast Implant is indicated for women at least 18 years old for the following:

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

CONTRAINDICATIONS

Breast implant surgery should not be performed in:

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

WARNINGS

There is a boxed warning for all breast implants (See Cover Page 1)

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

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

- Do not place drugs or substances in the implant other than sterile 0.9% Saline for Injection.
- Do not alter the implant or valves.
- Do not inject through the implant shell.
- Do not place more than one implant per breast pocket.
- Do not immerse the implant in povidone iodine solution or place povidone iodine solution in the implant. The pocket may be irrigated with a solution of equal parts povidone iodine and normal saline.
- Do not use endoscopic placement of the implant or peri-umbilical approach in placement of the implant.

Closed capsulotomy

Do not treat capsule 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.

Reuse

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

Avoiding damage during surgery

- Care should be taken not to damage the implant with surgical instruments.
- Do not insert or attempt to repair a damaged implant.
- Use care in subsequent procedures such as open capsulotomy, breast pocket revision, hematoma/Seroma aspiration, and biopsy/lumpectomy to avoid damage to

the implant shell or valves.
- Do not contact the implant with disposable, capacitor-type cautery devices.

Proper filling
Follow the recommended fill volumes shown in this Instruction for Use document; do not overfill or underfill the implant. Following recommended fill volumes may decrease the possibility of shell wrinkling and crease fold failure.

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

Surgical mesh
The use of surgical mesh together with the breast implant has not been studied in the clinical trial.

PRECAUTIONS

Safety and effectiveness has not been established in patients with the following:
- Autoimmune diseases such as lupus and scleroderma.
- A compromised immune system (for example, currently receiving immunosuppressive therapy).
- Conditions or medications which compromise or complicate wound healing or blood clotting.
- Inadequate tissue cover or reduced blood supply to breast tissue.
- Absent or substantially altered breast as a result of treatment for cancer or other pathologic conditions.
- Clinical diagnosis of depression or other mental health disorders, including body dysmorphic disorder and eating disorders. Please discuss any history of mental health issues with your patient prior to surgery. Patients with a diagnosis of depression, an anxiety disorder, or another mental health condition, should wait until resolution or stabilization of these conditions prior to undergoing breast implantation surgery.

Limited to use by physicians who have had training with breast implants.

IMPORTANT FACTORS TO BE DISCUSSED WITH THE PATIENT

Breast implantation is an elective procedure and the patient must be thoroughly counseled on the risks, as well as the benefits, of these products and procedures. You should advise your patient that she must read the Patient Information Booklet. The booklet is intended as the primary means to relate uniform risk and benefit information to assist your patient in making an informed decision about primary breast augmentation and revision of existing augmentation implants, but is not intended to replace consultation with you. The patient should review and consider this information before deciding whether to have this surgery.

Below are some of the important factors your patients need to be aware of when using Puregraft Serene breast implants (also see Patient Counseling on page 4):

- **Subsequent operation** – 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 lifetime devices, and they will likely undergo implant removal, with or without replacement, over the course of their life. Patients should be advised that the changes to their breast following explantation are irreversible.

- **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. Women should inform their mammographers about the presence of their implants.

- **Lactation** – Patients should be advised that the presence of breast implants may interfere with the ability to successfully breastfeed, either by reducing or eliminating milk production.

- **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.

- **Avoid Damage During Treatment** – Patients should inform other treating physicians of the presence of implants to minimize the risk of damage to the implants.

- **Smoking** – Smoking may interfere with the healing process.

- **Insurance Coverage** – Patients should be advised that health insurance premiums may increase, insurance coverage may be dropped, and/or future coverage may be denied based on the presence of breast implants. Treatment of complications may not be covered as well. Patients should check with their insurance company regarding coverage issues before undergoing surgery.

- **Mental Health and Elective Surgery** – It is important that all patients seeking to undergo elective surgery have realistic expectations that focus on improvement rather than perfection. Request that your patient openly discuss with you, prior to surgery, any history that she may have of depression or other mental health disorders.

INSTRUCTIONS FOR USE

NOTE: A backup implant should be available in the operating room. It is advisable to have more than one size implant available to allow for flexibility in determining the appropriate size implant to be used.

DO NOT stack more than one implant per breast pocket.

Sterilization
Implants are sterilized by dry heat and are single use only. Do not re-sterilize.

Implant Selection
Some of the important surgical and implant sizing variables that have been identified include the following:

- The implant should not be too small or too large in comparison to the patient's chest wall dimensions.
- Available tissue must provide adequate coverage of the implant.
- Submuscular placement of the implant may be preferable in patients with thin or poor quality tissue.
- A well-defined, dry pocket of adequate size and symmetry must be created to allow the implant to be placed flat on a smooth surface.
- An incision should be of appropriate length, about 4cm, to accommodate the implant and reduce excessive stress on the implant during insertion.

Testing Procedure for Saline-filled Implants
The implant should be tested for patency and shell integrity immediately prior to use. This can be accomplished by the following steps:

1. Partially inflate the implant with air through the fill tube.
2. Submerge the air-filled implant in sterile saline or water.
3. Apply mild pressure and check for possible leaks of the air inside.

Maintaining Hemostasis/Avoiding Fluid Accumulation
Careful hemostasis is important to prevent postoperative hematoma formation. Should excessive bleeding persist, the implantation should be delayed until bleeding is controlled. Postoperative evacuation of hematoma or seroma must be conducted with care to avoid breast implant contamination, or damage from sharp instruments.

Filling Procedure
Diaphragm valves are normally in the closed position. When the plug on the end of a fill tube is inserted into a valve, the diaphragm is held open, allowing the flow of air or saline. When the fill tube plug is removed, the diaphragm closes, sealing the valve. Overstressing the valve can cause damage such as punctures or tears and result in implant deflation. Use only the fill tube plug designed for and provided with this implant.

Since this implant has an inner lumen and an outer lumen that require different fill volumes (Table 2), the two respective fill tubes must not be confused once the implant is in the surgical pocket. For this reason, one fill tube is unmarked and is for the valve on the front of the implant while the other fill tube is marked: "**BACK---BIG---BEGIN**"

- **BACK** - for the valve on the **BACK** of the implant
- **BIG** - for the inner lumen that has a **BIG** fill volume compared to the outer lumen
- **BEGIN** - it is technically easier to **BEGIN** by filling the inner lumen and remove this fill tube from the back of the implant before filling the outer lumen from the front.

Remove and discard the protective strips between the valve straps and the valves. Wet the fill tube plugs in sterile isotonic saline for lubrication, slide the valve straps to one side and insert the plugs into the valve openings, using thumb and forefinger to stabilize the valves. While rotating slightly, gently push the fill tube plugs into the valve openings as far as the flanges permit. Be certain that the fill tube marked "**BACK---BIG---BEGIN**" is inserted into the valve on the **BACK** of the implant and the unmarked fill tube is inserted into the valve on the front of the implant.

When the valves are open, air will freely escape from both lumens as the implant is compressed. Attach a check valve to each luer lock and use an empty, sterile syringe to completely deflate each lumen. This minimizes the size of the implant for easier passage through the incision. Any remaining air in the implant will eventually diffuse out and be absorbed by the tissue. It is not necessary to remove the small amount of entrapped air. Remove the syringe, roll the implant, moisten it with saline for lubrication and insert it into the prepared pocket.

Use only sterile, pyrogen-free 0.9% Sodium Chloride U.S.P. Solution for Injection drawn from its original container, since infection may result from contaminated saline. For this reason, a closed injection system is recommended consisting of intravenous bag, intravenous tubing, 3-way stopcock and syringe. This closed system is connected to the sterile fill tubes supplied with the implant.

Follow Table 2 of this Instructions for Use document and the implant label for the recommended fill volumes of the inner lumen and the outer lumen. For each implant, the recommended fill volumes were calculated so they are proportionate to the implant size and the capacity of the inner and outer shells. This gives the implant optimal performance. Do not overfill or underfill the implant as this may cause wrinkles, scallops and/or deflation from crease/fold failure. When filling, allow for the 3cc of saline inside each fill tube.

BEGIN with the fill tube marked "**BACK---BIG---BEGIN**" that is inserted into the valve on the **BACK** of the implant for the **BIG** volume inner lumen. When the inner lumen is filled, remove its fill tube before using the unmarked fill tube that is inserted into the valve on the front of the implant for the small volume outer lumen. When the outer lumen is filled, remove its fill tube.

Use care when removing the fill tube plugs from the valves to prevent damage to the valve assemblies. Support the area around each valve with fingertips and pull the fill tube plug straight out, not at an angle to the valve. Position the valve strap over each valve and insert the protective strap plug into the valve opening.

Recording Procedure
Each breast implant is supplied with one Patient Implant Card and six Implant Record Labels showing the UDI, size and serial number for that implant. To complete the Patient Implant Card, adhere one Implant Record Label for each implant on the back of the Patient Implant Card. Another label should be affixed to the patient's chart. The Implant Record Label shows the empty implant volume and the inner lumen volume for that size implant. The implanted position (right or left side) should be indicated on the label as well as the volume of saline placed in the outer lumen. The total implant volume (the sum of the empty implant volume, the inner lumen volume, and the outer lumen volume) should be indicated on the label. This card belongs to the patient and should be given to her after surgery.

COMPLICATIONS

Potential adverse events that may occur with saline-filled breast implant surgery include: deflation, capsular contracture, reoperation, implant removal, pain, changes in nipple and breast sensation, infection, scarring, asymmetry, wrinkling, implant displacement/migration, implant palpability/visibility, breastfeeding complications, hematoma/seroma, implant extrusion, necrosis, delayed would healing, breast tissue atrophy/chest wall deformity, calcium deposits, and lymphadenopathy. For specific adverse event rates for Puregraft

Serene Breast Implant, refer to Safety Results on page 17. Below is a description of these adverse events:

- **Deflation** – Breast implants are not lifetime devices. Saline-filled breast implants deflate when the shell develops a tear or hole, or when a valve leaks. Deflation can occur any time after implantation, but is more likely to occur the longer the implant is in place. The following may cause deflation: damage by surgical instruments, folding or wrinkling of the implant shell, excessive force to the chest, compression during mammography, and severe capsule contracture. Breast implants may also simply wear out over time. Since this implant has two lumens, deflation of only one lumen will result in only partial deflation of the implant.

- **Reoperation** – Patients should be advised that additional surgery to their breast and/or implant will likely be necessary over the course of their life. Patients may decide to change the size or type of their implants, requiring a reoperation, or they may have a reoperation to improve or correct their outcome.

- **Capsular Contracture** – Patients should be advised that capsular contracture may be more common following infection, hematoma, and seroma, and the chance of it happening may increase over time. Capsular contracture occurs more commonly in revision augmentation patients than in primary augmentation patients. Capsular contracture is also a risk factor for implant deflation, and it is one of the most common reasons for reoperation.

  Patients should also be advised that additional surgery may be needed in cases where firmness is severe, ranging from removal of the implant capsule to replacement of the implant. Capsular contracture may recur following this additional surgery.

- **Implant Removal** – Patients should be advised that implants are not considered lifetime 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 implant removal are irreversible.

- **Infection** – In rare instances, acute infection may occur in a breast with implant. Signs of acute infection include erythema, tenderness, fluid accumulation, pain, and fever. Very rarely, Toxic Shock Syndrome (TSS), a potentially life-threatening condition, has been reported in women after breast implant surgery. Symptoms occur suddenly and include high fever (102^0 F, 38.8^0 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 contact a physician immediately for diagnosis and treatment of any of these symptoms.

- **Dissatisfaction with Cosmetic Results** – Patients should be informed that dissatisfaction with cosmetic results related to such things as scar deformity, capsule contracture, asymmetry, wrinkling, implant displacement/migration, incorrect size, and implant palpability/visibility 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. Revision surgery may be indicated to maintain patient satisfaction, but carries additional risks.

- **Breastfeeding** – Difficulties have been reported following breast augmentation surgery. A periareolar approach may further increase the chance of breastfeeding difficulties.

- **Additional Complications** – After breast implant surgery, the following may occur and/or persist, with varying intensity and/or for a varying length of time: pain, hematoma/seroma, changes in nipple and breast sensation, implant extrusion, necrosis, delayed would healing, and breast tissue atrophy/chest wall deformity. Calcium deposits can form in the capsule around the implant, resulting in pain and firmness. Lymphadenopathy has been reported in some patients.

OTHER REPORTED CONDITIONS

Patients receiving breast implants have reported a variety of systemic symptoms such as joint pain, muscle aches, confusion, chronic fatigue, autoimmune diseases, connective tissue diseases and others. Individual patient risk for developing these symptoms has not been well established. Some patients report complete resolution of symptoms when the implants are removed without replacement.

- **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.

- **Cancer** — Women with breast implants do not seem to have a greater risk of developing breast cancer (Brinton, et al 2006; Deapen, et al 2007). One exception is the rare development of Breast Implant Associated Anaplastic Large Cell Lymphoma (BIA-ALCL) a type of non- Hodgkin's lymphoma. in women with breast implants.

  - Based on information reported to global regulatory agencies and found in medical literature, an association has been identified between breast implants and the development of breast implant associated anaplastic large cell lymphoma (BIA-ALCL), a type of non- Hodgkin's lymphoma. Women with breast implants have a very small but increased risk of developing BIA-ALCL in the fluid or scar capsule adjacent to the implant, with documented potential for local, regional, and distant spread of the cancer with mortality reported in rare cases.

  - BIA-ALCL has been reported globally in patients with an implant history that includes various manufacturers' breast implants with various surface properties, styles, and shapes. Most of the cases in the literature for BIA-ALCL reports describe a history of the use of textured implants.

  - You should consider the possibility of BIA-ALCL when a patient presents with late onset, persistent peri-implant seroma. In some cases, patients presented with capsular contracture or masses adjacent to the breast implant. When testing for BIA-ALCL, collect fresh seroma fluid and representative portions of the capsule, and send to a laboratory with appropriate expertise for pathology tests to rule out ALCL, including immunohistochemistry testing for CD30 and ALK (anaplastic lymphoma kinase). If your patient is diagnosed with peri-implant BIA- ALCL, develop an individualized treatment plan in coordination with a multi- disciplinary care team.

Because of the small number of cases worldwide, there is no worldwide consensus on the treatment regimen for peri-implant BIA-ALCL. However, the National Comprehensive Cancer Network (NCCN) recommends surgical treatment that includes implant removal and complete capsulectomy ipsilaterally as well as contralaterally, where applicable.

- There have been reports of cancers, including squamous cell carcinoma (SCC) and various lymphomas, in the scar tissue (capsule) that forms around breast implants. The various lymphomas reported are not the same as the lymphomas as BIA-ALCL.

- Report all confirmed cases of BIA-ALCL, SCC, Other Lymphomas, and Other Cancers arising from the Capsule surrounding the breast implant to the FDA (https://www.fda.gov/Safety/MedWatch). In some cases, the FDA may contact you for additional information. The FDA will keep the identities of the reporter and the patient confidential.

- FDA also recommends reporting cases of BIA-ALCL, SCC, Other Lymphomas, and Other Cancers arising from the Capsule surrounding the breast implant to the PROFILE Registry https://www.thepsf.org/research/registries/profile where you can submit more comprehensive case data. This will help provide a better understanding of the etiology of these carcinomas and lymphomas.

For additional information on FDA's analysis and review of BIA-ALCL, please visit: https://www.fda.gov/medical-devices/breast-implants/medical-device-reports-breast-implant-associated-anaplastic-large-cell-lymphoma

- **Effects on Children** - There have been concerns raised regarding potential damaging effects on children born of mothers with implants. There is no evidence that shows breast implants have any harmful effects on the children of implanted women (Signorello, et al 2001; Kjoller, et al 2002).

PUREGRAFT SERENE BREAST IMPLANT 10-YEAR CLINICAL STUDY

SUMMARY OF THE STUDY METHODS

CLINICAL STUDY DESIGN AND OVERVIEW

Bimini Health Tech's Breast Implant Core Study is a prospective, 10-year, multi-center, open label study of the Puregraft Serene Breast Implant in which subjects serve as their own controls for the evaluation of effectiveness. Two patient cohorts were enrolled in the study:

- At least 18 year old women undergoing bilateral primary augmentation ("Primary Augmentation Cohort"); and

- At least 18 year old women undergoing bilateral revision of existing saline-filled or silicone gel-filled augmentation implants ("Revision" Augmentation Cohort").

STUDY VISITS AND LENGTH OF FOLLOW-UP

Within 30 days of the baseline visit, qualified subjects were implanted with Puregraft Serene Breast Implants. Patients returned for evaluation at 2 months, 6 months and 1 year, and

then annually for 10 years post-implant. At each follow-up visit, patients were examined, the implants assessed, the extent of capsule graded according to the Baker classification, and patient/investigator satisfaction assessed. At 6 months and 1 year, chest measurements were made. At 1, 2, 4, 6, 8 and 10 years, subjects completed the Breast Evaluation Questionnaire and the SF-36 Questionnaire. At 1, 2, 4, 7, and 10 years, subjects completed the Rheumatologic and Connective Tissue Disease Screen (CTDs). Adverse events were documented throughout the 10-year study. This study was conducted by Ideal Implant, Inc. with implants labeled with the Ideal Implant tradename. These names have been replaced with Bimini Health Tech and Puregraft Serene Breast Implant, respectively, to avoid confusion while reading this document.

STUDY OBJECTIVES and KEY STUDY ENDPOINTS

The objective of this study was to determine the safety and effectiveness of the Puregraft Serene Breast Implant in women undergoing primary breast augmentation or revision of existing saline- filled or silicone gel-filled augmentation implants. The safety study endpoint was that use of the Puregraft Serene Breast Implant elicits an acceptable safety profile. In general, the safety of the Puregraft Serene Breast Implant was assessed through the incidence and timing of all adverse events collected throughout the study.

Five effectiveness endpoints were evaluated:

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

TOTAL ENROLLED PATIENTS AND FOLLOW-UP RATE

The study enrolled 502 patients at 35 sites across the United States: 399 for primary breast augmentation and 103 for revision augmentation of existing saline or silicone gel augmentation implants. The study results through 10-years are presented here. Of the patients available to be seen for their 10-year follow-up visit, 342 of the primary augmentation patients (93%) and 84 of the revision augmentation patients (97%) returned and were seen at 10 years after implant surgery.

STUDY POPULATION: PATIENTS AND BASELINE DEMOGRAPHIC PROFILE

Table 3 shows the subject demographics and medical history for the women in the Primary Augmentation Cohort and the Revision Augmentation Cohort. Approximately 83% of patients were Caucasian. The median age of the primary augmentation patients was 34.0 years (range 18-68); the median age of the revision augmentation patients was 47.0 years (range 21-67).

Table 3 – Subject Demographics and Medical History, per Subject

Measure	Primary Augmentation (N=399)	Revision Augmentation (N=103)
Median Age Years [Minimum, Maximum] [1]	34.0 [18.0, 68.0]	47.0 [21.0, 67.0]

Table 3 – Subject Demographics and Medical History, per Subject		
Measure	**Primary Augmentation (N=399)**	**Revision Augmentation (N=103)**
Race[2]		
American Indian Alaska Native	1.3% (5/399)	0% (0/103)
Asian	3.0% (12/399)	1.9% (2/103)
Black / African American	5.0% (20/399)	1.9% (2/103)
Native Hawaiian / Pacific Islander	0.8% (3/399)	0% (0/103)
Caucasian	82.7% (330/399)	83.5% (86/103)
Other	9.5% (38/399)	14.6% (15/103)
Ethnicity		
Hispanic or Latino	11.8% (47/399)	14.6% (15/103)
Non-Hispanic or Latino	88.2% (352/399)	85.4% (88/103)
Median BMI [Minimum, Maximum] (kg/m^2)	21.6 [14.4, 53.2]	21.5 [18.1, 48.7]
Any Pregnancy History	73.9% (295/399)	89.3% (92/103)
Number of pregnancies *	2.6±1.4 (295) 2.0 [1.0, 8.0]	2.6±1.4 (92) 2.0 [1.0, 7.0]
Number of live births *	2.1±1.2 (295) 2.0 [0.0, 7.0]	2.0±1.0 (92) 2.0 [0.0, 5.0]

*Numbers are in the following formats: Mean ± standard deviation (SD) (N) and Median [Min, Max] for continuous measures.
[1] Age calculated at date of implant.
[2] More than one race category may be selected for each subject.

Early in the trial, the valve attachment diameter was increased from 6.3mm to 8mm. This was done to improve the bond strength, possibly reducing the risk of spontaneous deflation, and reducing the need for reoperation and implant removal. The number of subjects who had 6.3mm vs 8mm valve attachments in the clinical study is shown in Table 4. Additional modifications consisted of changing the baffle perforations from slits to holes late in the trial.

Table 4 - Kaplan-Meier Failure Rates for Adverse Events at 2 years for Initial Bilateral 6.3mm and Initial Bilateral 8mm Valve Attachment Component Implants, per Subject				
Event	**Primary Augmentation**		**Revision Augmentation**	
	6.3mm (N=31)	**8mm (N=363)**	**6.3mm (N=10)**	**8mm (N=93)**
All subsequent breast operations	32.3% (18.8%, 51.6%)	14.2% (11.0%, 18.3%)	50.0% (24.7%, 81.6%)	23.7% (16.3%, 33.7%)
Implant removal with or without Replacement	22.6% (11.5%, 41.6%)	7.5% (5.2%, 10.8%)	10.0% (1.5%, 52.7%)	15.1% (9.2%, 24.2%)
Spontaneous deflation	19.4% (9.2%, 38.1%)	4.8% (3.0%, 7.6%)	10.0% (1.5%, 52.7%)	3.3% (1.1%, 10.0%)

For the Primary Augmentation Cohort, 363 subjects were initially implanted with bilateral 8mm valve attachment component implants (355 had slit baffle perforations; 8 had hole

baffle perforations), 31 subjects received bilateral 6.3mm component implants (all had slit baffle perforations), and 5 subjects received a 6.3mm component implant on one side and a 8mm component implant on the other side (all had slit baffle perforations). A total of 391 subjects received slit baffle perforation implants and 11 subjects received hole baffle perforations implants.

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

Neither the 6.3mm diameter valve attachment component implant, nor the baffle hole perforations implant are available commercially.

Table 5 shows the operative details per implant for women in the Primary Augmentation and the Revision Augmentation Cohorts. The inframammary incision site was most common in both cohorts, and most implants were placed in the submuscular location. In the Primary Augmentation Cohort, 19.7% of the breasts had a concomitant procedure with mastopexy being the most common. More breasts in the Revision Augmentation Cohort underwent a concomitant breast procedure (74.8%), as expected, with 81.2% of those patients having a capsular procedure.

Table 5 - Surgical Operative Data, per Implant

Measure	Primary Augmentation (N=798)	Revision Augmentation (N=206)
Diameter valve attachment		
8mm	91.6% (731/798)	90.3% (186/206)
6.3mm[1]	8.4% (67/798)	9.7% (20/206)
Baffle perforations		
Slits	98.0% (782/798)	97.1% (200/206)
Holes[1]	2.0% (16/798)	2.9% (6/206)
Incision site		
Inframammary[2]	70.8% (565/798)	61.2% (126/206)
Periareolar	22.2% (177/798)	37.9% (78/206)
Axillary	7.0% (56/798)	1.0% (2/206)
Location		
Subglandular	8.0% (64/798)	19.4% (40/206)
Submuscular	92.0% (734/798)	80.6% (166/206)
Concurrent breast procedure	19.7% (157/798)	74.8% (154/206)
Capsule procedure	0% (0/157)	81.2% (125/154)
Mastopexy	91.7% (144/157)	26.0% (40/154)
Other[3]	8.3% (13/157)	18.8% (29/154)

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

[1] Design option not commercially available

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

[3] Other measures for primary augmentation were IMF repair, Correction of inverted nipples, Periareolar breast lift, Nipple reconstruction, Removal simple nipple benign growth (superficial), Bx -mass benign, Excise breast mass, Scar revision, Internal nipple lift, and Lipoma excised left chest wall. Other measures for revision augmentation were Breast reduction, Capsulectomy, Capsuloplasty, Capsulorrhaphy, Change to submuscular, Elevated Nipple - Areolar Complex, IMF repair, Lateral capsule repair, Mastopexy, Partial capsulotomy, Plicate lateral sulcus, Reduction, Removal ruptured silicone gel implant, and Scar revision breasts.

SUMMARY OF THE STUDY RESULTS

EFFECTIVENESS RESULTS

375 (94%) of the original 399 primary augmentation patients had a breast measurement at 1-year after surgery. Of these patients, the mean increase in chest circumference was 2.5 inches.

The Breast Evaluation Questionnaire, a validated instrument to assess satisfaction with breast attributes, was utilized to assess subjects' satisfaction with their breasts before and after surgery. Domains for this questionnaire were: satisfaction with breast attributes, comfort fully dressed, and comfort not fully dressed. Patients in the Primary Augmentation Cohort and the Revision Augmentation cohort experienced statistically significant increases from baseline in each domain of the Breast Evaluation Questionnaire at 1, 2, 4, 6, 8 and 10 years (t-test; p-value <0.001). At 10 years, patients in the Primary Augmentation Cohort reported: a mean of 54.2 (60 maximum score possible) on the Comfort Fully Dressed scale, a mean increase of 13.8 compared to the baseline; a mean of 97.1 (120 maximum score possible) on the Comfort Not Fully Dressed scale, a mean increase of 42.6 compared to the baseline; and a mean of 39.0 (45 maximum score possible) on the Satisfaction with Breast Attributes scale, a mean increase of 17.9 compared to the baseline. Subjects in the Revision Augmentation Cohort reported: a mean of 53.1 on the Comfort Fully Dressed scale, a mean increase of 6.3 compared to the baseline; a mean of 90.3 on the Comfort Not Fully Dressed scale, a mean increase of 17.0 compared to the baseline; and a mean of 38.5 on the Satisfaction with Breast Attributes scale, a mean increase of 8.5 compared to the baseline.

Patient and physician satisfaction with the overall cosmetic outcome were assessed using a five-point Likert scale, which ranged from definitely satisfied, somewhat satisfied, neither satisfied or dissatisfied, somewhat dissatisfied and definitely dissatisfied. At 10 years, 330 of the original 399 primary augmentation patients were included in an analysis of satisfaction and 79 of the original 103 revision augmentation patients were included in an analysis of satisfaction. Surgeons were definitely or somewhat satisfied with the outcomes in 94.8% (313/330) of the primary augmentation cases and in 87.3% (69/79) of the revision augmentation cases. In the Primary Augmentation Cohort, 92.7% (306/330) of patients were definitely or somewhat satisfied with the outcomes. In the Revision Augmentation Cohort, 82.3% (65/79) of patients were definitely or somewhat satisfied with the outcomes. The Physician and Patient Satisfaction with Outcome at 10 Years is shown in Table 6.

Table 6 - Physician and Patient Satisfaction with Outcome at 10 Years, per Patient

Cohort	Satisfaction Measure	10-Year Follow-up Visit	
		Primary Augmentation	Revision Augmentation
Physician Satisfaction	Physician definitely satisfied with outcome	81.2% (268/330)	72.2% (57/79)
	Physician somewhat satisfied with outcome with outcome	13.6% (45/330)	15.2% (12/79)
	Physician neither satisfied nor dissatisfied with outcome	0.9% (3/330)	0.0% (0/79)
	Physician somewhat dissatisfied with outcome	1.5% (5/330)	1.3% (1/79)
	Physician definitely dissatisfied with outcome	2.7% (9/330)	11.4% (9/79)
Subject	Subject definitely satisfied with outcome	81.5% (269/330)	74.7% (59/79)

Satisfaction	Subject somewhat satisfied with outcome with outcome	11.2% (37/330)	7.6% (6/79)
	Subject neither satisfied nor dissatisfied with outcome	2.7% (9/330)	1.3% (1/79)
	Subject somewhat dissatisfied with outcome	1.8% (6/330)	2.5% (2/79)
	Subject definitely dissatisfied with outcome	2.7% (9/330)	13.9% (11/79)
Numbers are Percent (Count/N). The 11 subjects with hole baffle shell perforations are excluded from effectiveness analyses as the hole baffle shell perforations design option is not commercially available. Both 6.3mm and 8mm valve attachment diameters are included in the effectiveness analyses although the 6.3mm design option is not commercially available.			

The SF-36v2® Health Survey was utilized to measure overall quality of life. The SF-36 measures eight scales: physical functioning (PF), role physical (RP), bodily pain (BP), general health (GH), vitality (VT), social functioning (SF), role emotional (RE), and mental health (MH). For all eight scales of the survey and at all time points, the mean SF-36 scores were clinically significantly higher for subjects compared to the general female population published within the SF-36v2 Health Survey User's Manual. Comparison of baseline scores to scores at 10 years show no clinically significant changes. There were a number of statistically significant decreases in certain quality of life scales. More importantly, these effect sizes were small or very small and therefore the observed changed were assessed not to be clinically relevant.

SAFETY RESULTS

The study safety results are presented in this section. Table 7 shows the 2-year, 5-year and 10-year Kaplan Meier (KM) risk rates of the first occurrence (95% confidence intervals) of adverse events for the two study cohorts per subject through 2 years, 5 years and 10 years. In the Primary Augmentation Cohort, complications occurring at a rate of ≥ 5% through 10 years included: all subsequent breast operations (39.4%), implant removal with or without replacement (32.1%), dissatisfaction with cosmetic results (11.4%), wrinkling/scalloping (9.0%), dissatisfaction with implant size selected (9.3%), capsular contracture – Grade III/IV (6.6%) and breast lesion – benign (6.6%). In the Revision Cohort, complications occurring at a rate of ≥ 5% through 10 years included: all subsequent breast operations (50.3%), implant removal with or without replacement (42.6%), wrinkling/scalloping (21.1%), capsular contracture – Grade III/IV (11.5%), dissatisfaction with implant size selected (13.6%), dissatisfaction with cosmetic results (15.6%), breast lesion – benign (7.6%) and breast ptosis – after implant procedure (6.2%).

Table 7 – Cumulative Kaplan-Meier Rates ≥ 1% for Adverse Events, per Patient

Event (Includes all levels of severity)	Primary Augmentation (N= 399)			Revision Augmentation (N=103)		
	2 yr	5 yr	10 yr	2 yr	5 yr	10 yr
All subsequent breast operations*	12.8% (9.8%,16.7%)	22.7% (18.7%, 27.5%)	39.4% (34.4%, 44.9%)	21.5% (14.5%, 31.4%)	39.3% (30.1%, 50.0%)	50.3% (40.4%, 61.1%)
Implant removal with or without replacement*	5.9% (3.9%, 8.8%)	14.9% (11.5%, 19.1%)	32.1% (27.4%, 37.5%)	12.9% (7.6%, 21.6%)	30.6% (22.2%, 41.2%)	42.6% (33.1%, 53.6%)
Connective Tissue Disease diagnosis	0.5% (0.1%, 2.1%)	0.8% (0.3%, 2.4%)	1.1% (0.4%, 2.8%)	0.0%	2.1% (0.5%, 8.2%)	2.1% (0.5%, 8.2%)

Reproductive problem	0.8% (0.3%, 2.4%)	1.3% (0.6%, 3.2%)	3.4% (1.9%, 5.9%)	0.0%	3.3% (1.1%, 9.8%)	3.3% (1.1%, 9.8%)
Other Adverse Event**	12.4% (9.5%, 16.1%)	21.3% (17.5%, 25.8%)	36.9% (32.1%, 42.1%)	14.0% (8.6%, 22.6%)	29.1% (21.1%, 39.3%)	42.6% (33.3%, 53.3%)
Capsular contracture Grade III/IV	3.8% (2.3%, 6.3%)	5.7% (3.8%, 8.5%)	6.6% (4.5%, 9.6%)	8.2% (4.2%, 15.8%)	11.5% (6.5%, 19.7%)	11.5% (6.5%, 19.7%)
Wrinkling/scalloping (excludes mild severity)	3.8% (2.3%, 6.3%)	7.3% (5.1%, 10.4%)	9.0% (6.5%, 12.4%)	12.0% (7.0%, 20.2%)	16.2% (10.3%, 25.2%)	21.1% (14.1%, 30.9%)
Spontaneous deflation*	0.3% (0.0%, 2.0%)	1.5% (0.6%, 3.5%)	3.7% (2.1%, 6.4%)	1.1% (0.2%, 7.4%)	4.7% (1.8%, 12.2%)	4.7% (1.8%, 12.2%)
Seroma	0.3% (0.0%, 1.8%)	0.3% (0.0%, 1.8%)	0.3% (0.0%, 1.8%)	2.9% (0.9%, 8.8%)	2.9% (0.9%, 8.8%)	4.1% (1.6%, 10.6%)
Dissatisfaction with cosmetic result	4.1% (2.5%, 6.6%)	7.8% (5.5%, 11.0%)	11.4% (8.5%, 15.2%)	8.9% (4.7%, 16.5%)	10.0% (5.5%, 17.7%)	15.6% (9.7%, 24.5%)
Hematoma/bleeding	1.8% (0.8%, 3.6%)	1.8% (0.8%, 3.6%)	1.8% (0.8%, 3.6%)	0.0%	0.0%	0.0%
Wound Healing delay/tissue necrosis/dehiscence	1.3% (0.5%, 3.0%)	1.3% (0.5%, 3.0%)	1.5% (0.7%, 3.4%)	1.0% (0.1%, 6.7%)	1.0% (0.1%, 6.7%)	1.0% (0.1%, 6.7%)
Wound Infection	1.3% (0.5%, 3.0%)	1.3% (0.5%, 3.0%)	1.3% (0.5%, 3.0%)	1.0% (0.1%, 7.0%)	1.0% (0.1%, 7.0%)	1.0% (0.1%, 7.0%)
Implant exposure/extrusion	0.0%	0.0%	0.3% (0.0%, 2.0%)	2.0% (0.5%, 7.8%)	2.0% (0.5%,7.8%)	2.0% (0.5%, 7.8%)
Skin scar unsatisfactory	1.5% (0.7%, 3.4%)	1.5% (0.7%, 3.4%)	1.5% (0.7%, 3.4%)	3.9% (1.5%, 10.1%)	3.9% (1.5%, 10.1%)	3.9% (1.5%, 10.1%)
Mastopexy unsatisfactory	1.5% (0.7%, 3.4%)	1.5% (0.7%, 3.4%)	2.1% (1.1%, 4.2%)	1.1% (0.2%, 7.3%)	2.2% (0.5%, 8.4%)	2.2% (0.5%, 8.4%)
Implant position unsatisfactory (malposition)	2.6% (1.4%, 4.7%)	2.8% (1.6%, 5.1%)	3.4% (2.0%, 5.8%)	1.0% (0.1%, 6.7%)	3.2% (1.0%, 9.5%)	3.2% (1.0%, 9.5%)
Persistent breast pain	0.5% (0.1%, 2.0%)	1.0% (0.4%, 2.8%)	1.0% (0.4%, 2.8%)	1.1% (0.1%, 7.2%)	1.1% (0.1%, 7.2%)	1.1% (0.1%, 7.2%)
Inadequate milk supply	0.3% (0.0%, 1.8%)	1.6% (0.7%, 3.5%)	3.3% (1.9%, 5.8%)	1.1% (0.2%, 7.3%)	1.1% (0.2%, 7.3%)	1.1% (0.2%, 7.3%)
Dissatisfaction with implant size selected	3.0% (1.7%, 5.3%)	7.0% (4.9%, 10.0%)	9.3% (6.5%, 13.1%)	3.9% (1.5%, 10.1%)	10.2% (5.6%, 18.2%)	13.6% (8.1%, 22.4%)
Breast ptosis - after implant procedure	0.5% (0.1%, 2.0%)	2.1% (1.1%, 4.2%)	4.4% (2.7%, 7.1%)	4.1% (1.5%, 10.4%)	5.1% (2.2%, 11.9%)	6.2% (2.9%, 13.4%)
Breast lesion – benign	1.5% (0.7%, 3.4%)	4.3% (2.6%, 6.9%)	6.6% (4.5%, 9.7%)	4.1% (1.6%, 10.5%)	5.2% (2.2%, 12.0%)	7.6% (3.7%, 15.4%)
Breast lesion – malignant	0.5% (0.1%, 2.0%)	0.8% (0.3%, 2.4%)	1.6% (0.7%, 3.6%)	0.0%	1.1% (0.2%, 7.4%)	1.1% (0.2%, 7.4%)

* Kaplan-Meier rates for Subsequent breast operation, Implant removal, and Spontaneous deflation are based upon analyses of subjects whose initial bilateral surgery included implants with the final valve attachment design (8 mm valve) , N=363 for Primary Augmentation Cohort and N=93 for Revision Augmentation Cohort. For the rest of the rates, they are based on a combination of 6.3mm valve and 8mm valve attachment components.
**Other adverse events: For the Primary Augmentation Cohort: breast tissue atrophy, interference with mammography, nipple/breast sensitivity change, mastitis, lactation pain, lymphadenopathy, melanoma arm, seasonal allergy, squamous cancer skin, nasal polyps, seizure disorder, bowel obstruction, hemorrhoids, irritable bowl syndrome, hypothyroidism, hyperthyroidism, emotional issue, neck rash, abdominal muscle bleed, rotator cuff problem, cholecystitis, foot fracture, contact dermatitis, back pain, tubular breast, liver cyst, herpes zoster infection, syncopal episode, myasthenia gravis, staph infection nose, leukemia, cervical cancer, anxiety, cystitis, diabetes, depression, acid reflux, head trauma, migraine, urinary retention, drug overdose, borderline personality disorder, anal fissure, arm cyst, abdominal incision pain, cold, herniated disc, enlarged thymus, kidney infection, rectal prolapse, abdominal wound infection, basal cell carcinoma nose, arm pain, sinus infection, nausea, ovarian cancer, eczema arms and renal stone. For the Revision Augmentation Cohort: sciatic neuritis, sebaceous cysts of scalp, sinus obstruction, renal stone, seroma to abdomen, abdominal wound infection, anemia, ganglion cyst thigh, femoral hernia, hand numbness, multiple sclerosis, stasis ulcer ankle, pancreatic cancer, superficial burn, intra-arterial septal communication, cholecystitis, sleep apnea, depression, rash abdomen, EKG abnormality, back pain, diverticulitis, lipoma hip, hyperthyroidism, whooping cough and knee trauma.

REASONS FOR SUBSEQUENT BREAST OPERATIONS (REOPERATIONS)

There were 179 subsequent breast operations performed in 134 Primary Augmentation Cohort patients and 77 subsequent breast operations performed in 45 Revision Augmentation Cohort patients through 10 years. The cumulative primary reasons for subsequent breast operations (reoperations) through 2 years, 5 years and 10 years in the Primary Augmentation Cohort and the Revision Augmentation Cohort are summarized in Table 8.

Table 8 - Cumulative Primary Reasons for Subsequent Breast Operation
(Data are for Bilateral 8mm Subjects)

Reason	Primary Augmentation			Revision Augmentation		
	2 Year	5 Year	10 Year	2 Year	5 Year	10 Year
Capsular contracture (II)	5.4% (3/56)	5.8% (6/104)	5.6% (10/179)	3.0% (1/33)	3.4% (2/59)	2.6% (2/77)
Capsular contracture (III-IV)	8.9% (5/56)	8.7% (9/104)	6.1% (11/179)	3.0% (1/33)	6.8% (4/59)	7.8% (6/77)
Wrinkling/scalloping	5.4% (3/56)	4.8% (5/104)	5.6% (10/179)	12.1% (4/33)	8.5% (5/59)	10.4% (8/77)
Spontaneous deflation	1.8% (1/56)	2.9% (3/104)	6.7% (12/179)	3.0% (1/33)	1.7% (1/59)	1.3% (1/77)
Other related to presence of implant*	1.8% (1/56)	10.6% (11/104)	24.6% (44/179)	0.0%	5.1% (3/59)	10.4% (8/77)
Hematoma/bleeding	5.4% (3/56)	2.9% (3/104)	1.7% (3/179)	0.0%	0.0%	0.0%
Healing delay/necrosis/dehiscence	3.6% (2/56)	1.9% (2/104)	1.1% (2/179)	0.0%	0.0%	0.0%
Infection (peri-prosthetic)	0.0%	0.0%	0.0%	6.1% (2/33)	3.4% (2/59)	2.6% (2/77)
Implant exposure/extrusion	0.0%	0.0%	0.6% (1/179)	24.2% (8/33)	13.6% (8/59)	10.4% (8/77)
Skin scar unsatisfactory	3.6% (2/56)	1.9% (2/104)	1.1% (2/179)	0.0%	0.0%	0.0%
Mastopexy unsatisfactory	5.4% (3/56)	3.8% (4/104)	2.8% (5/179)	0.0%	1.7% (1/59)	1.3% (1/77)
Implant position unsatisfactory	8.9% (5/56)	4.8% (5/104)	2.8% (5/179)	0.0%	1.7% (1/59)	1.3% (1/77)
Other related to procedure	1.8% (1/56)	1.0% (1/104)	0.6% (1/179)	3.0% (1/33)	3.4% (2/59)	2.6% (2/77)
Dissatisfaction with implant size	12.5% (7/56)	15.4% (16/104)	13.4% (24/179)	12.1% (4/33)	11.9% (7/59)	13.0% (10/77)
Breast ptosis prior to implant placement	5.4% (3/56)	2.9% (3/104)	2.2% (4/179)	0.0%	1.7% (1/59)	1.3% (1/77)
Breast ptosis after implant placement due to pregnancy, change in weight, and/or change in breast size	1.8% (1/56)	2.9% (3/104)	2.2% (4/179)	0.0%	1.7% (1/59)	3.9% (3/77)
Breast lesion – benign or malignant	3.6% (2/56)	5.8% (6/104)	5.0% (9/179)	0.0%	1.7% (1/59)	1.3% (1/77)

Breast reconstruction post trauma/cancer	0.0%	1.0% (1/104)	0.6% (1/179)	3.0% (1/33)	3.4% (2/59)	2.6% (2/77)
Inadequate saline volume	14.3% (8/56)	10.6% (11/104)	6.1% (11/179)	18.2% (6/33)	10.2% (6/59)	7.8% (6/77)
Absence of implant	0.0%	0.0%	0.0%	3.0% (1/33)	1.7% (1/59)	1.3% (1/77)
Dissatisfaction with cosmetic result	1.8% (1/56)	1.9% (2/104)	1.1% (2/179)	9.1% (3/33)	5.1% (3/59)	5.2% (4/77)
Other**	8.9% (5/56)	10.6% (11/104)	10.1% (18/179)	0.0%	11.9% (7/59)	11.7% (9/77)

Numbers are Percent (Count/N)
Denominator is the number of subsequent breast operations prior to the upper end of the visit window. One primary reason is summarized per operation. Subsequent breast operations were performed in 134 primary augmentation patients and 45 revision augmentation patients through 10 years.
If both implants were operated on and had different reasons, the primary reason was selected followed the FDA guideline hierarchy.
* Reasons under this category for primary augmentation are cosmetic (asymmetry, irregularities with knuckling, desire for larger size, wide sternum or deformity, matching replacement implant, asymmetrical deflation). Reasons under this category for revision augmentation are cosmetic (asymmetry), and dissatisfaction with feel of implant.
** Reasons under this category for primary augmentation are cosmetic (asymmetry, cosmetic dissatisfaction, dissatisfaction with overall breast size, tubular breast anatomy), preference (implants no longer desired, silicone implants desired, elective exchange in conjunction with exchange of defective side, replaced to match other implant, dissatisfaction with feel of implants), crunchy implant feel, fat grafting, thin breast tissue, and not specified. Reasons under this category for revision augmentation are cosmetic (asymmetry), preference (implants no longer desired, felt strange), crunchy implant feel, resection cyst IMF, abrasion open area, and replacement with new implant of this same brand.

REASONS FOR IMPLANT REMOVAL

The cumulative primary reasons for implant removal with or without replacement through 2 years, 5 years and 10 years are provided in Table 10 for the Primary Augmentation Cohort and the Revision Augmentation Cohort. There were 157 implants removed from patients in the Primary Augmentation Cohort and 68 implants removed from patients in the Revision Augmentation Cohort. The Cumulative Primary Reasons for Implant Removal are shown in Table 9.

Table 9 - Cumulative Primary Reasons for Implant Removal, per Implant
(Data are for Bilateral 8mm Subjects)

Reason Category	Primary Augmentation			Revision Augmentation		
	2 Year	5 Year	10 Year	2 Year	5 Year	10 Year
Capsular contracture (II)	3.4% (1/29)	2.7% (2/74)	3.2% (5/157)	4.5% (1/22)	6.7% (3/45)	4.4% (3/68)
Capsular contracture (III-IV)	10.3% (3/29)	8.1% (6/74)	3.8% (6/157)	4.5% (1/22)	13.3% (6/45)	11.8% (8/68)
Wrinkling/scalloping	3.4% (1/29)	5.4% (4/74)	7.0% (11/157)	9.1% (2/22)	4.4% (2/45)	11.8% (8/68)
Spontaneous deflation	3.4% (1/29)	4.1% (3/74)	7.6% (12/157)	4.5% (1/22)	2.2% (1/45)	1.5% (1/68)
Other related to presence of implant*	0.0%	13.5% (10/74)	33.8% (53/157)	0.0%	8.9% (4/45)	13.2% (9/68)
Healing delay/necrosis/dehiscence	3.4% (1/29)	1.4% (1/74)	0.6% (1/157)	0.0%	0.0%	0.0%
Infection (peri-prosthetic)	0.0%	0.0%	0.0%	4.5% (1/22)	2.2% (1/45)	1.5% (1/68)
Implant exposure/extrusion	0.0%	0.0%	0.6% (1/157)	18.2% (4/22)	8.9% (4/45)	5.9% (4/68)
Implant position unsatisfactory (malposition)	0.0%	0.0%	0.6% (1/157)	0.0%	0.0%	0.0%
Dissatisfaction with implant size	44.8% (13/29)	36.5% (27/74)	22.9% (36/157)	27.3% (6/22)	22.2% (10/45)	20.6% (14/68)
Breast ptosis prior to implant	0.0%	0.0%	1.3% (2/157)	0.0%	0.0%	0.0%

Breast ptosis after implant due to pregnancy, change in weight, and/or change in breast size	0.0%	0.0%	0.0%	0.0%	0.0%	2.9% (2/68)
Breast lesion – benign or malignant	3.4% (1/29)	1.4% (1/74)	1.3% (2/157)	0.0%	0.0%	0.0%
Breast reconstruction post trauma/cancer	0.0%	1.4% (1/74)	0.6% (1/157)	0.0%	0.0%	0.0%
Dissatisfaction with cosmetic result	6.9% (2/29)	5.4% (4/74)	2.5% (4/157)	27.3% (6/22)	13.3% (6/45)	8.8% (6/68)
Other**	20.7% (6/29)	20.3% (15/74)	14.0% (22/157)	0.0%	17.8% (8/45)	17.6% (12/68)

Numbers are Percent (Count/N)
Denominator is the number of implants removed (with or without replacement).
* Reasons under this category for primary augmentation are cosmetic (asymmetry within breast, asymmetry between breasts, irregularities with knuckling, desire for larger size), and pain in one breast and lump. Reasons under this category for revision augmentation are cosmetic (asymmetry within breast, asymmetry between breasts), and dissatisfaction with feel of implant.
** Reasons under this category for primary augmentation are cosmetic (asymmetry within breast, asymmetry between breasts, cosmetic dissatisfaction), preference (implants no longer desired, requests removal, silicone implants desired, elective exchange in conjunction with exchange of defective side), preventive mastectomy, dissatisfaction with feel of implants. Reasons under this category for revision augmentation are cosmetic (asymmetry between breasts), preference (implants no longer desired), dissatisfaction with feel of implants, and replacement with new implant of this same brand

OTHER CLINICAL DATA FINDINGS

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

Breast Disease

In the Primary Augmentation Cohort through 10 years, there were 28 reports of abnormal mammogram findings: 2 breast cancer, 9 benign breast lesions or masses, 2 calcification, 7 cysts, 1 fibroadenoma, 1 engorged breasts, 3 ruptured implant, 1 dense breasts, 1 scarring and 1 additional evaluation necessary. In the Revision Augmentation Cohort through 10 years, there were 8 reports of abnormal mammogram findings: 1 cyst, 3 calcifications, 2 masses and 2 additional evaluation necessary.

Breast Implant Associated - Anaplastic Large Cell Lymphoma

Through 10 years, there were no reports of breast implant associated anaplastic large cell lymphoma (BIA-ALCL) in any patient.

Connective Tissue/Autoimmune Disease (CTD)

Patients underwent a screening for connective tissue disorders at each follow-up visit. Approximately 4% (N=14) of the patients in the Primary Augmentation Cohort and 1% (N=1) of the patients in the Revision Augmentation Cohort were referred to a board certified Rheumatologist at the 10 year visit. The risk of an initial diagnosis of CTD through 10 years was 1.1% for patients in the Primary Augmentation Cohort and 2.1% for patients in the Revision Augmentation Cohort.

Lactation and Reproduction Problems

The risk of inadequate milk supply through 10 years was 3.3% for patients in the Primary Augmentation Cohort and 1.1% for patients in the Revision Augmentation Cohort. In the Primary Augmentation Cohort, 12 patients had a reproductive problem of which 9 were

miscarriages, 1 was patient diagnosed with endometriosis and underwent laparoscopic lysis of adhesions and removal of some endometriosis, 1 was a non-viable birth, and the other unknown. In the Revision Augmentation Cohort, 3 patients experienced a reproductive problem of which 2 were miscarriages, the other was unknown.

Suicide
There were no reports of suicide in either cohort through 10 years.

Deaths and Unanticipated Adverse Device Effects

There was one death reported in the Primary Augmentation Cohort; a patient died of cervical cancer. There were two patient deaths reported in the Revision Augmentation Cohort: one case of cardiopulmonary arrest and one case of pancreatic cancer.

There were no unanticipated adverse device effects in either the Primary Augmentation Cohort or the Replacement Augmentation Cohort .

CONCLUSIONS FROM CLINICAL STUDY

EFFECTIVENESS CONCLUSIONS

The effectiveness outcomes demonstrate that the majority of patients who underwent a chest measurement (primary augmentation cohort only) report an increase in chest circumference. The majority of patients who provided Breast Evaluation Questionnaire assessments at the 1, 2, 4, 6, 8 and 10-year assessments point had favorable results. The majority of patients who provided a satisfaction rating at 10 years indicated that they were satisfied with their breast implants. The majority of physicians who provided a satisfaction rating at 10 years reported being satisfied with the breast implants. Comparison of baseline SF-36 scores to scores at 1, 2, 4, 6, 8 and 10 years show no clinically significant changes.

SAFETY CONCLUSIONS

The risks of the device are based on nonclinical laboratory and/or animal studies as well as data collected in a clinical study conducted to support PMA approval as described above. The most common complications through 10 years were subsequent breast operations, implant removal with or without replacement, capsular contracture, wrinkling/scalloping, dissatisfaction with implant size selected, and dissatisfaction with cosmetics results.

STUDY STRENGTHS AND WEAKNESSES

Bimini Health Tech’s clinical study had a number of strengths. The study was prospective and multi-centered, with a large number of sites (35), a large number of patients (502), a 10 years follow-up period and high follow-up rates (≥ 93%). The study also included two categories of patients for which use of the implant is approved: primary augmentation and revision augmentation. Adding to the strengths of this study were the long term, investigations of both the safety and effectiveness of the implant, based on assessments made by both the surgeons and by enrolled patients. These assessments, which are shared throughout this IFU, represent a comprehensive and consistent evaluation of the known or suspected safety risks that women undergoing breast implantation surgery may encounter from both a physician and patient perspective. Weaknesses of the study included the

study's open-label nature and lack of a control group. Furthermore, it should be noted that this study was not designed to detect rare events that may occur in women undergoing breast implantation surgery. Important to note is that the results of the study are descriptive in nature and may not be able to be generalized to a larger population, nor do they necessarily represent all possible postoperative complications that a woman undergoing breast implantation surgery can expect.

BENEFIT-RISK CONCLUSIONS

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

Additional factors to be considered in determining probable risks and benefits for the Puregraft Serene Breast Implant device included: the active and deliberate search/documentation of adverse events in the clinical study, single arm pivotal study design, lacking individual patient success criteria, good patient follow-up through 10 years, the availability of alternative treatments, patient-centric assessments, and risk mitigation with device use by trained surgeons in patients with informed consent.

In conclusion, given the available information above, the data support that the probable benefits outweigh the probable risks for women for Puregraft Serene Breast Implant for the following procedures:

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

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:

- Patient Information Booklet (Making an Informed Decision Puregraft Serene Breast Implant Breast Implant Surgery)

  This booklet 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 at least a week after reviewing and considering this information before deciding whether to have augmentation surgery.

- Patient Decision Checklist

  After the material in the Patient Information Booklet is read, reviewed, discussed and understood, the patient and physician should initial and/or sign the Checklist where indicated and receive a copy for future reference to this information.

- National Breast Implant Registry (NBIR)

In collaboration with the U.S. Food and Drug Administration (FDA), breast implant device manufacturers, and patients, The Plastic Surgery Foundation (PSF) has developed the National Breast Implant Registry (NBIR) for the purpose of strengthening national surveillance for breast implant devices in the United States. The NBIR is a database that collects information on breast implant procedures and devices. Collecting this information will allow the NBIR, plastic surgeons, and breast implant manufacturers to identify trends and other helpful safety information that can be used to improve the safety of breast implants for you and future patients. You are encouraged to participate in this registry.

- Patient Implant Card

  Each breast implant is supplied with a Patient Implant Card and six Implant Record Labels. To complete the Patient Implant Card, place one Implant Record Label for each implant on the back of the card. If a label is unavailable, the serial number and size of the implant may be copied by hand from the implant label. This card belongs to the patient and should be given to her for personal reference.

  The patient implant card contains the following information:
  - A statement that “This card belongs to the patient. Please give it to the patient.”
  - Device’s serial or lot number.
  - Device’s style and size.
  - Unique Device Identifier (UDI).
  - Web link to access most current patient decision checklist, boxed warning, and labeling for the specific implant that the patient received.
  - A statement that “There is a boxed warning for breast implants, see web link.”
  - Toll-free phone number to the breast implant manufacturer.

ADDITIONAL PRODUCT INFORMATION

EXPLANT RETURN

The reason for explantation should be reported and the explant returned to Bimini Health Tech, Product Evaluation Department, 8400 Belleview Drive, Suite 125, Plano, TX 75024 for examination and analysis. Call 858-348-8050 for instructions and shipping information.

DEVICE TRACKING

Breast Implants are subject to device tracking under the Food and Drug Administration (FDA) regulation 21 CFR §821.30. Tracking is intended to facilitate notifications to patients of important new information about a device as it becomes available. The laws governing device tracking require physicians to report the below information relating to their practice, the breast implants used, and the patients who receive breast implants. Upon implantation a physician is required to promptly provide Bimini Health Tech with the following information:

- The name, mailing address, and telephone number of the implanting physician;
- The serial number of the breast implant;
- The date the breast implant was implanted;
- The name, address, telephone number, and social security number (if available) of the patient receiving the device, unless the patient has refused the released of this information for tracking purposes;

- The name, mailing address, and telephone number of the physician regularly following the patient if different than the implanting physician; and

When applicable, the date the device was explanted and the name, mailing address, and telephone number of the explanting physician, the date of the patient's death, or the date the device was returned to the manufacturer, permanently retired from use, or otherwise permanently disposed of.

PRODUCT EVALUATION

Bimini Health Tech requires that any serious complications resulting from use of this implant be brought to the immediate attention of Bimini Health Tech, Product Evaluation Department, 8400 Belleview Drive, Suite 125, Plano, TX 75024.

RETURNED GOODS POLICY

Implants returned must have the shrink wrap seal intact and must be returned within 6 months from date of shipping to be eligible for credit or replacement. Please contact Bimini Health Tech for details.

LIMITED WARRANTY

The Bimini Health Tech Breast Implant Limited Warranty provides lifetime replacement in the event of implant failure, subject to certain conditions as described in the Breast Implant Limited Warranty posted on puregraft.com/serene. For more information, contact Bimini Health Tech.

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