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direction for use

SIENTRA SILICONE GEL BREAST IMPLANTS

SMOOTH ROUND,
TEXTURED ROUND AND
TEXTURED SHAPED

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 approved labeling provided by Sientra, Inc.

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

WARNING:

- Breast implants are not considered lifetime devices. The longer people 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 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.

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INTRODUCTION

DIRECTIONS TO THE PHYSICIAN

The information contained in this *Directions for Use* (DFU) is intended to provide an overview of essential information about Sientra Silicone Gel Breast Implants (also referred to as the "Implants") including a device description, the indications for use, contraindications, warnings, precautions, important factors for a patient to consider, adverse effects, other reported conditions, and a summary of the Sientra Clinical Study of Silicone Gel Breast Implants (also referred to as the "Study"). There is a **Boxed Warning** for all breast implants (See Cover Page).

Patient Counseling Information
You should review this document and the patient labeling, including the *Patient Decision Checklist* that highlights key information regarding risks of breast implant surgery, prior to counseling the patient about Sientra Silicone Gel 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 the use of this device. You should thoroughly review all of the risk information with the patient and address all of her questions prior to signing the Checklist along with the patient, indicating that you have reviewed all of the information and addressed all of her questions. As with any surgical procedure, breast implantation is not without risks. Breast implantation is an elective procedure, and the patient must be well counseled and understand the risk/benefit relationship.

Before making the decision to proceed with surgery, you should instruct the patient to read the document titled: *Patient Educational Brochure: Breast Augmentation/Reconstruction with Sientra Silicone Gel Breast Implants* (patient labeling), and discuss with the patient the warnings, precautions, important factors to consider, complications, and the Study results listed in the patient labeling. You should advise the patient of the potential complications and that medical management of serious complications may include additional surgery and explantation.

Please refer to the *INFORMATION TO BE DISCUSSED WITH THE PATIENT* section of this document for additional patient counseling information.

Informed Decision
Each patient should receive Sientra's *Patient Educational Brochure: Breast Augmentation/Reconstruction with Sientra Silicone Gel Breast Implants* during the patient's initial visit/consultation, to allow the patient sufficient time to read and adequately understand the important information on the risks, follow-up recommendations, and benefits associated with silicone gel breast implant surgery.

Allow the patient at least 1-2 weeks to review and consider this information before deciding to have primary breast surgery. In the case of revision surgery, it may be necessary to perform surgery sooner.

In order to document a successful informed decision process, as discussed above the patient labeling includes a *Patient Decision Checklist*, which should be signed by both the patient and the surgeon and then retained in the patient's file. A copy should also be provided to the patient.

Device Tracking
Silicone Gel Breast Implants are subject to device tracking per Food and Drug Administration (FDA) regulation. Tracking is intended to facilitate notifying patients in the event that important new information about a device becomes available. The laws that govern device tracking require physicians to report certain information relating to their practice, the breast implants used, and the patients who receive breast implants (21 CFR §821.30).1 A physician prescribing Silicone Gel Breast Implants is required, by federal regulation, to comply with Device Tracking Regulations, and report to Sientra:

- The serial number of the implanted device(s),
- The date of the implant surgery,
- Patient's name,
- The patient's personal contact information (including address, telephone number and date of birth),
- Contact information for the prescribing physician's practice and the physician who regularly sees the patient for primary care, and
- (When applicable) the date the device was:
    - Explanted, with the name, mailing address, and telephone number of the explanting physician;
    - Out of use due to patient death (date of death);
    - Returned to the manufacturer;
    - Permanently disposed of.

Tracking continues until the implant is returned, destroyed, explanted, or the patient becomes deceased. Tracking information will be recorded on the **Device Tracking Form** supplied by Sientra with each Implant. The form should then be returned to Sientra via fax.

Sientra strongly recommends that all patients receiving Sientra's Implants participate in Sientra's Device Tracking program.

Patients are not required by law to enroll themselves in any tracking program or device registry. However, participation in Sientra's Device Tracking program is required in order to activate the Sientra Limited Warranty discussed in the *PRODUCT REPLACEMENT POLICY AND LIMITED WARRANTIES* section of this DFU. Patients must allow their physicians to share contact information and information about the implant in order to activate the Warranty.

DEVICE DESCRIPTION

Sientra Implants are single-lumen devices composed of a barrier-type, silicone elastomer shell, filled with high-strength silicone gel. The Implants are dry heat sterilized and are available in various shapes, profiles, and sizes.

TABLE 1. shows available styles and sizes of Sientra's Silicone Gel Breast Implants.

Style Number and Gel Filler		Shell Surface	Shape and Profile	Volume (cc)	Width (cm)	Height (cm)	Projection (cm)
HSC	HSC+						
10512-MP	10712-MP	Smooth	Round Moderate	80-700	8.1-16.1	8.1-16.1	2.1-4.7
10521-HP	10722-HP	Smooth	Round High	95-695	8.2-15.4	8.2-15.4	2.5-4.9
20612-MP	20712-MP	Textured	Round Moderate	80-700	8.1-16.1	8.1-16.1	2.1-4.7
10610-LP	10710-LP	Smooth	Round Low	60-700	7.3-17.9	7.3-17.9	2.1-3.8
20610-LP	20710-LP	Textured	Round Low	60-700	7.3-17.9	7.3-17.9	2.1-3.8
10621-MP/HP	10721-MP/HP	Smooth	Round Moderate/ High	95-700	7.7-15.1	7.7-15.1	2.9-6.0
10621-XP	10721-XP	Smooth	Round Extra High	190-510	8.75-12.0	8.75-12.0	4.6-6.2
20621-MP/HP	20721-MP/HP	Textured	Round Moderate/ High	95-700	7.7-15.1	7.7-15.1	2.9-6.0
20621-XP	20721-XP	Textured	Round Extra High	190-510	8.75-12.0	8.75-12.0	4.6-6.2
N/A	20645-LP	Textured	Shaped Inferior Pole Low	170-700	11.3-17.4	9.8-14.9	2.8-4.5
N/A	20645-MP/HP	Textured	Shaped Inferior Pole Moderate/ High	120-700	8.9-16.9	8.0-14.5	3.4-6.2
N/A	20646-RB (MP)	Textured	Shaped Inferior Pole Moderate	160-700	9.2-15.5	9.2-15.5	4.0-6.1
N/A	20646-RB (HP)	Textured	Shaped Inferior Pole High	180-550	9.8-14.6	8.3-13.4	4.3-6.2
N/A	20676-E (MP)	Textured	Shaped Superior Pole Moderate	115-700	8.0-16.1	9.0-17.2	3.2-5.8
N/A	20676-E (HP)	Textured	Shaped Superior Pole High	190-635	9.0-14.0	10.0-15.0	4.2-6.2

INDICATIONS FOR USE

Sientra Silicone Gel Breast Implants are indicated for:

- **Breast augmentation for women at least 22 years old.** Breast augmentation includes primary breast augmentation as well as revision surgery to correct or improve the result of primary breast augmentation surgery.
- **Breast reconstruction**. Breast reconstruction includes primary reconstruction to replace breast tissue that has been removed due to cancer or trauma or that has failed to develop properly due to a severe breast abnormality. Breast reconstruction also includes revision surgery to correct or improve the results of a primary breast reconstruction surgery.

CONTRAINDICATIONS

Breast implant surgery is contraindicated in women

- With active infections anywhere in their body,
- With existing cancer or precancerous conditions who have not received adequate treatment for those conditions,
- Who are currently pregnant or nursing.

WARNINGS

AVOID DAMAGING THE IMPLANT DURING SURGERY AND OTHER MEDICAL PROCEDURES

WARNING:

- Breast implants are not considered lifetime devices. The longer people 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 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.

The most common causes of implant rupture include damage to the implant that occurs during the surgical implantation or other related medical procedures. Accordingly, physicians should not use excessive force and should minimize the handling of the implant during surgical insertion.

- Do not allow cautery devices or sharp instruments, such as scalpels, suture needles, hypodermic needles, hemostats, Adson forceps or scissors to contact the Implant during the implantation procedures.
- Use an appropriate length incision to accommodate the style, size, and profile of the implant.
- Do not treat capsular contracture by closed capsulotomy or forceful external compression, which could likely result in implant damage, rupture, folds, and/or hematoma.
- Use care in subsequent procedures, such as open capsulotomy, breast pocket revision, hematoma/seroma aspiration, and biopsy/lumpectomy to avoid damage to the implant. Repositioning of the implant during surgical procedures should be carefully evaluated by the medical team and care taken to avoid contamination of the implant. Use of excessive force during any subsequent procedure can contribute to localized weakening of the breast implant shell potentially leading to decreased device performance.
- Do not immerse the implant in any liquid such as Betadine or other iodine solution. If Betadine is used in the pocket, ensure that it is rinsed thoroughly so that no residual solution remains in the pocket.
- Do not alter the implants or attempt to repair or insert a damaged implant.
- Do not reuse or re-sterilize any implant that has been previously implanted. Breast implants are intended for single use only.
- Do not place more than one implant per breast.
- Do not use the periumbilical approach to place this implant.

MICROWAVE DIATHERMY

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

PRECAUTIONS

SPECIFIC POPULATIONS

The safety and effectiveness of this device have not been established in patients with

- Autoimmune diseases,
- A compromised immune system (for example, currently receiving immunosuppressive therapy),
- Conditions that interfere with wound healing and blood clotting,
- Reduced blood supply to breast tissue,
- Chemotherapy or radiation to the breast following implantation, and
- Clinical diagnosis of depression or other mental disorders, including body dysmorphic disorder and eating disorders. Please discuss any history of mental health disorders with your patient prior to surgery. Patients with a diagnosis of depression or other mental disorders should wait until resolution or stabilization of these conditions prior to undergoing breast implantation surgery.

In order to avoid possible injury or damage to the incision site(s), you should advise your patients to avoid the following for the first month after the surgery:

- Sun exposure,
- Jerky movements or activities that stretch the skin at your incision site(s),
- Participating in sports or other activities that raise your pulse or blood pressure,
  and
- Unnecessary physical or emotional stress.

SURGICAL PRECAUTIONS

Surgical precautions, such as those described below, should be undertaken to maximize a successful aesthetic result and the long-term performance of the device.

Surgical Technique
The implantation of Sientra Silicone Gel Breast Implants involves a variety of surgical techniques. Therefore, you should use the method, which in your own best medical judgment, will provide the patient with the desired outcome consistent with this *Directions for Use* document.

Implant Selection
In order to properly select the correct implant, the following considerations should be taken into account and, as appropriate, discussed with the patient:

- The implant should be consistent in size with the patient's chest-wall dimensions, including base width measurements, also considering the laxity of the tissue and the projection of the implant.
- A thorough discussion should be conducted with the patient, employing appropriate visual aids to clarify her objectives and manage expectations, in order to reduce the incidence of reoperation for size change.
- The following may cause implants to be more palpable: larger implants, subglandular placement, and an insufficient amount of skin/tissue available to cover the implant.
- Available tissue must provide adequate coverage of the implant.

Incision Site Selection
You should choose one of the following incision sites, based on your patient's particular needs:

- The periareolar incision
- The inframammary incision
- The axillary incision

The periumbilical approach has not been studied in Sientra's Study and should not be used for a variety of reasons, including potential damage to the implant shell.

Implant Placement Selection
A well-defined, dry pocket of adequate size and symmetry must be created for implant placement.

Possible benefits of submuscular placement are that it may result in less palpable implants, less likelihood of capsular contracture (2000)[2], and easier imaging of the breast for mammography. Also, submuscular placement may be preferable if the patient has thin or weakened breast tissue.

Subglandular placement may result in more palpable implants, greater likelihood of capsular contracture (2004-2005),[3,4] and increased difficulty in imaging the breast with mammography.

INFORMATION 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 labeling for either augmentation or reconstruction, as applicable. The patient labeling 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-augmentation, or primary reconstruction and revision-reconstruction surgery (as applicable), but is not intended to replace consultation with you. The patient should be advised to wait at least 1-2 weeks after reviewing and considering this information before deciding whether to have this surgery, unless an earlier surgery is deemed medically necessary.

Both you and your patient will be required to sign the *Patient Decision Checklist* form prior to surgery. This form can be found on the last page of each patient brochure. The form, once signed, acknowledges the patient's full understanding of the information provided in the brochure. The form should be retained in the patient's permanent medical record.

Below are some of the important factors your patients need to be aware of when using Sientra Implants.

RUPTURE

Rupture of a silicone gel breast implant may be silent/asymptomatic (i.e., there are no symptoms experienced by the patient and no physical signs of changes with the implant), rather than symptomatic. You should advise your patient to undergo regular breast ultrasound or magnetic resonance imaging (MRI) to screen for silent rupture even if she is asymptomatic. For asymptomatic patients, the first ultrasound or MRI should be performed at 5-6 years postoperatively, then every 2-3 years thereafter. For symptomatic patients or patients with equivocal ultrasound results for rupture at any time postoperatively, an MRI is recommended. If rupture is noted on imaging, then you should advise your patient to have her Implant removed. You should provide her with a list of MRI facilities in her area that have at least a 1.5 Tesla magnet, a dedicated breast coil, and a radiologist experienced with reading breast implant MRIs to diagnose a silent rupture. Diagnostic procedures will add to the cost of having implants, and patients should be aware or advised that these costs may exceed the cost of their initial surgery over their lifetime and that their insurance carrier may not cover these costs.

EXPLANTATION

Implants are not considered lifetime devices, and patients will likely undergo implant removal(s), with or without replacement, over the course of their life. When implants are removed without replacement, changes to the patient's breasts may be irreversible. Complication rates are typically higher following revision surgery (removal with replacement).

REOPERATION

Additional surgeries to the patient's breasts will likely be required, whether because of implant rupture, other complications, or unacceptable size/cosmetic outcomes. Patients should be advised that their risk of future complications increases with revision surgery as compared to primary augmentation or reconstruction surgery. Further, in a reoperation in which the implant is not removed (such as open capsulotomies or scar revision), there is a risk that the integrity of the implant's shell could be compromised inadvertently, potentially leading to product failure.

BREAST EXAMINATION TECHNIQUES

Patients should perform breast self-examinations monthly and be shown how to distinguish the implant from their breast tissue. The patient should not manipulate or squeeze the implants excessively. The patient should be told that the presence of lumps, persistent pain, swelling, hardening, or change in the implant shape might be symptoms of rupture of the implant. If the patient has any of these signs, the patient should be told to report them to her surgeon, and possibly have an MRI evaluation to screen for rupture.

MAMMOGRAPHY

Patients should be instructed to undergo routine mammography exams as per their primary care physician's recommendations. The importance of having these exams should be emphasized. Patients should be instructed to inform their mammography technologist about the presence, type, and placement of their implants. Patients should request a diagnostic mammography, rather than a screening mammography, because more pictures are taken with diagnostic mammography. Breast implants may complicate the interpretation of mammographic images by obscuring underlying breast tissue and/or by compressing overlying tissue. Accredited mammography centers, technicians with experience in imaging patients with breast implants, and the use of displacement techniques, are needed to adequately visualize breast tissue in the implanted breast. The current recommendations for preoperative/screening mammograms are no different for women with breast implants than for those women without implants. Pre-surgical mammography with a follow-up mammogram after implantation may be performed to establish a baseline for routine future mammography in augmentation patients.

LACTATION

Breast implant surgery may interfere with the ability to successfully breast feed, either by reducing or eliminating milk production. The Institute of Medicine (IOM), in its 1999 report on the safety of silicone breast implants, encourages mothers with silicone gel breast implants to breast feed, stating that while breast implantation may increase the risk of lactation difficulties, there is no evidence of a hazard to the infant "beyond the loss of breastfeeding itself", (2000).[2] Other professional medical associations and independent scientific panels have echoed these conclusions and recommendations (1996,1998, 2001).[5-7]

AVOIDING DAMAGE DURING OTHER TREATMENT

Patients should inform other treating physicians of the presence of implants to minimize the risk of damage to the implants.

SMOKING

As with any surgery, smoking may interfere with the healing process after breast implant surgery.

RADIATION TO THE BREAST

Sientra 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 (2006,2009),[8,9] necrosis, and implant extrusion (2009).[10]

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 of breast implantation 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.

LONG-TERM EFFECTS

Sientra will continue its Study through the end of each patient's 10-year study term. In addition, Sientra has initiated a separate dual-design postapproval study, which includes a prospective cohort study and a series of case-control studies, to address specific issues that Sientra's current Study was not designed to fully answer, as well as to provide a real-world assessment of key endpoints. The endpoints in Sientra's dual-design postapproval study include long-term local complications, connective tissue disease (CTD), CTD signs and symptoms, neurological disease, neurological signs and symptoms, offspring issues, reproductive issues, lactation issues, cancer, including BIA-ALCL, suicide, mammography issues, and MRI compliance and results. Sientra will update its product labeling on a regular basis with the results of these studies. It is important for you to relay any new safety information to your patients as soon as such information is provided to you.

GENERAL ADVERSE EFFECTS ASSOCIATED WITH BREAST IMPLANT SURGERY

Potential adverse events that may occur with silicone gel breast implant surgery include: rupture, capsular contracture, reoperation, implant removal, pain, changes in nipple and breast sensation, infection, hematoma/seroma, unsatisfactory results, breast feeding complications and additional complications.

Below is a description of these adverse events. For specific adverse event rates/outcomes for Sientra Implants, refer to the Study section that follows.

RUPTURE

Breast implants are not lifetime devices. Breast implants rupture when the shell develops a tear or hole. Rupture can occur any time after implantation, but rupture is more likely to occur the longer the implant is implanted. The following things may cause implants to

rupture: damage by surgical instruments; stressing the implant during implantation and weakening it; folding or wrinkling of the implant shell; excessive force to the chest; trauma; compression during mammographic imaging; and severe capsular contracture. Breast implants may also simply wear out over time.

Silicone gel breast implant ruptures may be silent. This means that it is possible that neither you nor your patient will know if the implant has ruptured. Asymptomatic patients should have their first ultrasound or magnetic resonance imaging (MRI) performed at 5-6 years postoperatively, then every 2-3 years thereafter. Symptomatic patients or patients with equivocal ultrasound results for rupture at any time postoperatively, an MRI is recommended.

Studies (1992,1995-1996) in the medical literature suggest that silent rupture is relatively uncommon.[11-13] These symptoms include hard knots or lumps surrounding the implant or in the armpit, change or loss of size or shape of the breast or implant, pain, tingling, swelling, numbness, burning, or hardening of the breast (2001-2003).[14-17]

When MRI findings indicate a rupture (such as subcapsular lines, characteristic folded wavy lines, teardrop sign, keyhole sign, noose sign), or ultrasound findings of rupture or if there are signs or symptoms of rupture, you should remove the Implant (with or without replacement of the Implant) and any gel you determine is present. It also may be necessary to remove the tissue capsule, as well, all of which will involve additional surgery, with associated costs. If your patient has symptoms, such as breast hardness, a change in breast shape or size, and/or breast pain, you should recommend that she have an MRI to determine whether rupture is present (2000, 2004).[2,18]

There may also be consequences of rupture. If rupture occurs, silicone may either remain within the scar tissue surrounding the Implant (intracapsular rupture) or move outside the capsule (extracapsular rupture), or gel may move beyond the breast (migrated gel). There is also a possibility that rupture that initially occurs as an intracapsular rupture may progress to extracapsular and beyond. There have been few health consequences associated with migrated gel reported in the literature.

Additional Information on the Consequences of Rupture from Literature:

Studies of Danish women evaluated with MRI involving a variety of manufacturers and implant models showed that about three-fourths of implant ruptures are intracapsular and the remaining one-fourth is extracapsular (2001)[19]. Additional studies of Danish women indicate that over a 2-year period, about 10% of the implants with intracapsular rupture progressed to extracapsular rupture as detected by MRI (2004).[18] Approximately half of the women whose ruptures had progressed from intracapsular to extracapsular reported that they experienced trauma to the affected breast during this time period or had undergone mammography. In the other half, no cause was given. In the women with extracapsular rupture, after 2 years, the amount of silicone seepage outside the scar tissue capsule increased for about 14% of these women. This type of information pertains to a variety of silicone implants from a variety of manufacturers and implant models, and is not specific to Sientra's Silicone Gel Breast Implants.

CAPSULAR CONTRACTURE

Patients should be advised that capsular contracture might be more common following infection, hematoma, and seroma, and that the chance of it occurring may increase over time. Capsular contracture is also a risk factor for implant rupture (2001),[15] and it is one of the most common reasons for reoperation. Patients should be advised that additional surgery might be needed in cases where pain and/or firmness are severe. This surgery ranges from removal of the implant capsule tissue to removal and possible replacement of the implant itself. This surgery may result in loss of breast tissue. Capsular contracture may recur after these additional surgeries.

REOPERATION

Patients should be advised that additional surgery to their breast and/or implant will likely be necessary over the course of their life. Reoperations can be required for many reasons including a patient's decision to change the size or type of her implants, or to otherwise improve her breast surgery outcome.

IMPLANT REMOVAL

Patients should be advised that the 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 explantation might be irreversible.

PAIN

Pain of varying intensities and lengths of time may occur and persist following breast implant surgery. In addition, improper size, placement, surgical technique, or capsular contracture may result in pain. The surgeon should instruct his or her patient to inform him or her if there is significant pain or if pain persists.

CHANGES IN NIPPLE AND BREAST SENSATION

Sensation in the nipple and breast can increase or decrease after implant surgery.

Sensation is typically lost after complete mastectomy where the nipple itself is removed. This loss of feeling can be severely lessened by partial mastectomy. Radiation therapy also can significantly reduce sensation in the remaining portions of the breast or chest wall. The placement of breast implants for reconstruction may further lessen the sensation in the remaining skin or breast tissue. The range of changes varies from intense sensitivity to no feeling in the nipple or breast following surgery. While some of these changes can be temporary, they can also be permanent, and may affect the patient's sexual response or ability to 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), vomiting, diarrhea, a sunburn-like rash, red eyes, dizziness, lightheadedness, muscle aches, and drops in blood pressure, which may cause fainting. Patients should be instructed to contact a physician immediately for diagnosis and treatment for any of these symptoms.

UNSATISFACTORY RESULTS

Patients should be informed that dissatisfaction with cosmetic results related to such things as incorrect size, scar deformity, hypertrophic scarring, capsular contracture, asymmetry, wrinkling, implant displacement/migration, and implant palpability/visibility might occur. Careful surgical planning or 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 considerations and risks.

BREAST FEEDING COMPLICATIONS

Difficulties with breast-feeding have been reported following both breast reduction and breast augmentation surgeries. A periareolar surgical approach may further increase the chance of breast feeding difficulties.

ADDITIONAL COMPLICATIONS

After breast implant surgery, the following may occur and/or persist, with varying intensity and/or varying length of time: implant extrusion, necrosis, delayed wound healing, and breast tissue atrophy/chest wall deformity. Calcium deposits can form in the tissue capsule surrounding the implant with symptoms that may include pain and firmness. Lymphadenopathy has also been reported in some women with implants.

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 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.

There have been reports in the literature of other conditions in women with silicone gel breast implants. Many of these conditions have been studied to evaluate their potential association with breast implants. Furthermore, there is the possibility of risks, yet unknown, which in

the future could be determined to be associated with breast implants. It should be noted that the cited references include data from augmentation and/or reconstruction patients, as well as from a variety of manufacturers and implant models.

CONNECTIVE TISSUE DISEASE DIAGNOSES OR SYNDROMES

Connective tissue diseases include diseases such as lupus, scleroderma, rheumatoid arthritis and fibromyalgia. There have been a number of published epidemiological studies, meta-analyses, and "weight-of-the-evidence" or critical reviews that have looked at whether having a breast implant is associated with having a typical or defined connective tissue disease. The study size needed to conclusively rule out a smaller risk of connective tissue disease among women with silicone gel breast implants would need to be very large (2000, 2003-2004).[2,20-25] Some published studies (1997-2002, 2004) taken together show that breast implants are either not significantly associated with a risk of developing a typical or defined connective tissue disease, or if a significance was detected, based on limitations of the studies a causative relationship with breast implants could not be determined.[2,14,15,22-24,26-34] These studies do not distinguish between women with intact and ruptured implants. One study (2003) evaluated specific connective tissue disease diagnoses and symptoms in women with silent ruptured versus intact implants, but it was too small to rule out a small risk.[21] Another study(2003) in a small group of women concluded that significantly more women with ruptured implants than intact implants reported debilitating chronic fatigue;[35] the women reported their symptoms after learning whether or not they had a ruptured implant.

Some independent scientific panels and review groups have concluded that there is no evidence to support an association between breast implants and connective tissue disease or at least, if a risk cannot be absolutely excluded it is too small to be quantified (1998 and 2000-2001).[2,7,24]

CONNECTIVE TISSUE DISEASE SIGNS AND SYMPTOMS

Some literature reports have also been made associating silicone gel breast implants with various rheumatological signs and symptoms, such as fatigue, exhaustion, joint pain and swelling, muscle pain and cramping, tingling, numbness, weakness, and skin rashes. Having these rheumatological signs and symptoms does not necessarily mean that a patient has a connective tissue disease. Some scientific expert panels (2000) and literature reports (2001-2002 and 2004) have found no evidence of a consistent pattern of signs and symptoms in women with silicone gel breast implants.[2,36-39] If a patient has an increase in these signs or symptoms, you should refer her to a rheumatologist to determine whether these signs or symptoms are due to a connective tissue disorder or autoimmune disease.

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.

CANCER

Breast Cancer

Some reports (2000-2001,2006-2007) in the medical literature indicate that patients with breast implants are not at a greater risk than those without breast implants for developing breast cancer.[27,40-48] Some reports (2000,2002-2004) have suggested that breast implants may interfere with or delay breast cancer detection by mammography and/or biopsy; however, other reports in the published medical literature indicated that breast implants neither significantly delay breast cancer detection nor adversely affect cancer survival of women with breast implants.[21,40,43,48-50]

Brain and Nervous System Cancers

One study has reported an increased risk of brain cancer in women with breast implants as compared to the general population (2001).[41] The incidence of brain cancer, however, was not significantly increased in women with breast implants when compared to women who had other types of plastic surgeries; the study relied on very few cases and the authors relied upon death certificates for brain cancer diagnoses, which may reflect other cancers that have metastasized. Other large studies (2000, 2002, 2004, 2006-2007) and a published review of four large studies in women with cosmetic implants concluded that the evidence does not support an association between brain cancer and breast implants.[23,42,44-48]

Lympho-Hematopoietic Cancers
One study (2001) has reported an increased risk of leukemia in women with breast implants as compared to the general population.[41] However, there was no increased risk when compared to women who had other types of plastic surgery. Other recent large studies (2000, 2002, 2004, 2006-2007) concluded that the evidence does not support an association between lympho-hematopoietic cancers and breast implants.[23,42,44-48]

Breast Implant Associated-Anaplastic Large Cell Lymphoma (BIA-ALCL)
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 anaplastic large cell lymphoma (BIA-ALCL), a type of non-Hodgkin's lymphoma (2008).[51] Women with breast implants have a very small but increased risk of developing ALCL (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 Sientra's and other manufacturers' breast implants with various surface properties, styles, and shapes. Most of the cases in the literature 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 BIA-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 multidisciplinary 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.

Report all confirmed cases of BIA-ALCL 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 to the PROFILE Registry (https://www.thepsf.org/research/clinical-impact/profile.htm) where you can submit more comprehensive case data. This will help provide a better understanding of the etiology of BIA-ALCL.

For additional information on FDA's analysis and review of the BIA-ALCL please visit: http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/ImplantsandProsthetics/BreastImplants/ucm239995.htm

Respiratory/Lung Cancer
One study (2001) has reported an increased incidence of respiratory/lung cancer in women with breast implants.[41] Other research (2006) in women in Sweden and Denmark have found that women who get breast implants are more likely to be current smokers than women who get breast reduction surgery or other types of cosmetic surgery.[46] Several large studies (2002, 2006-2007) have found no association between breast implants and respiratory/lung cancer.[42,44,45,47,48]

Reproductive System Cancers
One study (2001) has reported an increased incidence of cervical/vulvar cancer in women with breast implants.[41] However, there was no increased risk when compared to women who had other types of plastic surgery. Another study (2007) reported an increased incidence of vulvar cancer that has not been explained.[44] Other recent large studies (2000, 2002, 2004, 2006) concluded that the evidence does not support an association between reproductive system cancers and breast implants.[23,42,45-48]

Other Cancers
There have been several studies published that examined the risk of other types of cancers, e.g., thyroid cancers, urinary system cancers, sarcoma, endocrine cancer connective tissue cancer, cancer of the eye, and unspecified cancers in women with breast implants. All of those studies found no increased risk in women with breast implants(2000-2001, 2003-2004, 2006-2007).[17,37,41,42,44-47]

NEUROLOGICAL DISEASE, SIGNS, AND SYMPTOMS

Some women with breast implants have complained of neurological symptoms (such as difficulties with vision, sensation, muscle strength, walking, balance, thinking, or remembering things) or neurological diseases (such as multiple sclerosis), which they believe are related to their implants. One scientific expert panel(2000) found that the evidence for a neurological disease or syndrome caused by or associated with breast implants is insufficient or flawed.[2] Subsequent to that report, one epidemiological study (2001)[52] and one cohort study (2001)[27] examined a variety of neurological diseases in women with breast implants and found no significantly increased risk.

SUICIDE

In several studies(2001-2004), a higher incidence of suicide, depression, and/or anxiety was observed in women with breast implants.[53-57] The reason for the observed increase is unknown, but it was found that women with breast implants had higher rates of hospital admissions due to psychiatric causes prior to surgery, as compared with women who had breast reduction or in the general population of Danish women.[55]

EFFECTS ON CHILDREN

It is not known if a small amount of silicone may pass through from the breast implant silicone shell into breast milk during breast-feeding. Although there are no current established methods for accurately detecting silicone levels in breast milk, a study (2000) measuring silicon (one component of silicone) levels did not indicate higher levels in breast milk from women with silicone gel breast implants when compared to women without implants (based on literature published from 2000.[58]

In addition, concerns have been raised regarding potential damaging effects on children born to mothers with implants. Several studies (2001-2002, 2006) in humans have found that the risk of birth defects or other adverse health effects overall is not increased in children born after breast implant surgery.[59-61] Although low birth weight was reported in one study (2004), other factors (for example, lower pre-pregnancy weight) may explain this finding.[62] This author recommended further research on infant health.

POTENTIAL HEALTH CONSEQUENCES OF GEL BLEED

Small quantities of low molecular weight (LMW) silicone compounds, as well as platinum (in zero oxidation state), have been found to diffuse ("bleed") through an intact implant shell (2000, 2003).[2,63] The evidence is inconclusive as to whether there are any clinical consequences associated with gel bleed. For instance, studies on implanted women over a long duration have suggested that such bleed may be a contributing factor in the development of capsular contracture (2000)[2] and lymphadenopathy (2005).[64] However, evidence against gel bleed being a significant contributing factor to capsular contracture and other local complications, is provided by the fact that there are similar or lower complication rates for silicone gel breast implants than for saline-filled breast implants. Saline-filled breast implants do not contain silicone gel, and, therefore, gel bleed is not an issue for those products. Furthermore, toxicology testing has indicated that the silicone material used in the Study implants does not cause toxic reactions when large amounts are administered to test animals. It should also be noted that studies reported in the literature have demonstrated that the low concentration of platinum contained in breast implants is in the zero oxidation (most biocompatible) state (1987, 1995, 1999).[65-68]

Sientra performed a laboratory test to analyze the silicones and platinum (used in the manufacturing process), which may bleed out of intact implants into the body. Over 99% of the LMW silicones and platinum stayed in the implant. The overall body of available evidence supports that the extremely low level of gel bleed is of no clinical consequence.

SIENTRA'S CLINICAL STUDY

OVERVIEW

Sientra's Silicone Gel Breast Implant Clinical Study (called the "Study") is a prospective, 10-year, multicenter clinical study conducted to examine the safety and effectiveness of Sientra's Silicone Gel Breast Implant in patients undergoing primary augmentation, primary reconstruction, revision-augmentation, and revision-reconstruction of the breast. The Study consists of data from the primary augmentation

and revision-augmentation cohorts of Sientra's CORE study, as well as pooled data from Sientra's CORE and Continued Access (CA) studies for the primary reconstruction and revision-reconstruction cohorts.

There are 1,788 patients participating in the Clinical Study. A total of 1,115 patients had primary augmentation, 362 patients had revision-augmentation, 229 patients had primary reconstruction (156 CORE and 73 CA) and 82 patients (50 CORE and 32 CA) had revision reconstruction with Sientra Implants. Of these patients, 230 primary augmentation patients, 74 revision-augmentation patients, 34 primary reconstruction patients, and 7 revision-reconstruction patients are assessed for implant rupture by MRI at years 3, 4, 6, 8, and 10 years. Assessment of the safety of the Study Implants was based on the incidence of complications, including device failures, and assessment of effectiveness was based on changes in bra size/chest circumference and patient-reported quality-of-life (QOL) outcomes, including the Short Form Health Survey (SF-36), the Rosenberg Self-Esteem Scale, and the Body Image Scale.

Data through 3 years are available for 80% of the eligible primary augmentation patients, 79% of the eligible revision-augmentation patients, 83% of the eligible primary reconstruction patients, and 76% of the revision-reconstruction patients. Table 2 provides a tabulation of patient accounting.

TABLE 2. Patient accounting

Follow-up Year	Study Cohort			
	Primary Augmentation	Revision Augmentation	Primary Reconstruction	Revision Reconstruction
Year 1				
Theoretically Due	1,115	362	229	82
Discontinued (Deaths & Explants)	4 (0 & 4)	7 (0 & 7)	13 (1 & 12)	6 (0 & 6)
Other Discontinued (Not Avail & Subject Request)	1 (1 & 0)	1 (0 & 1)	2 (0 & 2)	0 (0 & 0)
Expected	1,110	354	214	76
Lost to Follow-up	93	37	18	9
Actual Evaluated (% Follow-up)	1017 (92 %)	317 (90 %)	196 (92 %)	67 (88 %)
Year 2				
Theoretically Due	1,115	362	229	82
Discontinued (Deaths & Explants)	13 (0 & 13)	15 (1 & 14)	15 (1 & 14)	12 (1 & 11)
Other Discontinued (Not Avail & Subject Request)	3 (1 & 2)	1 (0 & 1)	3 (0 & 3)	0 (0 & 0)
Expected	1,099	346	211	70
Lost to Follow-up	173	50	32	9
Actual Evaluated (% Follow-up)	926 (84 %)	296 (86 %)	179 (85 %)	61 (87 %)
Year 3				
Theoretically Due	1,115	362	229	82
Discontinued (Deaths & Explants)	21 (0 & 21)	19 (1 & 18)	17 (3 & 14)	14 (2 & 12)
Other Discontinued (Not Avail & Subject Request)	4 (1 & 3)	2 (0 & 2)	3 (0 & 3)	1 (0 & 1)
Expected	1,090	341	209	67
Lost to Follow-up	222	71	35	16
Actual Evaluated (% Follow-up)	868 (80 %)	270 (79 %)	174 (83 %)	51 (76 %)

Demographic information for the Study with regard to race is as follows: 92% of the Study patients were Caucasian; 3% were Hispanic; 2% were Asian, 2% were African American; less than 1% were Indian and less than 2% were other or unknown. The median age at surgery was 36 years for primary augmentation patients, 42 years for revision-augmentation patients, 46 years for primary reconstruction patients, and 50 years for revision-reconstruction patients. Approximately 59% of the Study patients were married. Approximately 74% had some college education. Table 3 presents the Study population demographics at baseline by cohort.

TABLE 3. Patient Demographics by Cohort

Characteristic	Primary Augmentation N=1,115	Revision Augmentation N=362	Primary Reconstruction N=229	Revision Reconstruction N=82 struction
Age (years)				
≤ 21	47 (4.2%)	3 (0.8%)	8 (3.5%)	0 (0%)
22-25	102 (9.1%)	12 (3.3%)	5 (2.2%)	0 (0%)
26-39	565 (50.7%)	127 (35.1%)	57 (24.9%)	8 (9.8%)
40-49	334 (30.0%)	139 (38.4%)	67 (29.3%)	26 (31.7%)
50-59	58 (5.2%)	63 (17.4%)	63 (27.5%)	28 (34.1%)
60-69	8 (0.7%)	18 (5.0%)	17 (7.4%)	14 (17.1%)
70 & over	1 (0.1%)	0 (0%)	11 (4.8%)	6 (7.3%)
Not provided	0 (0%)	0 (0%)	1 (0.4%)	0 (0%)
Median Age	36 years	42 years	46 years	50 years
Marital Status				
Single	317 (28.4%)	91 (25.1%)	48 (21.0%)	14 (17.1%)
Married	640 (57.4%)	217 (59.9%)	145 (63.3%)	57 (69.5%)
Widowed	9 (0.8%)	9 (2.5%)	6 (2.6%)	5 (6.1%)
Divorced	126 (11.3%)	42 (11.6%)	26 (11.4%)	6 (7.3%)
Separated	21 (1.9%)	3 (0.8%)	1 (0.4%)	0 (0%)
Not Provided	2 (0.2%)	0 (0%)	3 (1.3%)	0 (0%)
Race				
Caucasian	1,013 (90.9%)	337 (93.1%)	208 (90.8%)	78 (95.1%)
Black	12 (1.1%)	7 (1.9%)	5 (2.2%)	2 (2.4%)
Hispanic	37 (3.3%)	7 (1.9%)	10 (4.4%)	1 (1.2%)
Asian	29 (2.6%)	8 (2.2%)	1 (0.4%)	0 (0%)
Indian	1 (0.1%)	0 (0%)	1 (0.4%)	0 (0%)
Other	22 (2.0%)	2 (0.6 %)	2 (0.9%)	1 (1.2 %)
Not Provided	1 (0.1%)	1 (0.3 %)	2 (0.9%)	0 (0%)
Education				
Less than 12 years	8 (0.7%)	4 (1.1%)	5 (2.2%)	1 (1.2%)
High School Graduate	187 (16.8%)	68 (18.8%)	72 (31.4%)	23 (28.0%)
Some College	368 (33.0%)	94 (26.0%)	53 (23.1%)	24 (29.3%)
College Graduate	398 (35.7%)	150 (41.4%)	63 (27.5%)	21 (25.6%)
Post Graduate	94 (8.4%)	26 (7.2%)	18 (7.9%)	6 (7.3%)
Not Provided	60 (5.4%)	20 (5.5%)	18 (7.9%)	7 (8.5%)

With respect to surgical approach, for primary augmentation patients, the majority of implants (62%) were placed through an inframammary incision; 34% of implants were placed through a periareolar incision. The placement was submuscular in 57% of implants and subglandular in 43% of implants. Round implants represented 89% of total implants and shaped implants represented 12% of total implants. Smooth implants represented 58% of implants and textured implants represented 42% of implants.

For revision-augmentation patients, the majority of implants (61%) were placed through an inframammary incision; 34% of implants were placed through a periareolar incision. The placement was submuscular in 61% of implants and subglandular in 39% of implants. Round implants represented 86% of implants and shaped implants represented 14% of implants. Smooth implants represented 47% of implants and textured implants represented 53% of implants.

For primary reconstruction patients, the most commonly used surgical approach for implant placement (45%) was through a mastectomy or other scar, 29% were placed through an inframammary incision, and 16% of implants were placed through a periareolar incision. The placement was submuscular in 73% of implants and subglandular in 27% of implants. Round implants represented 88% of implants and shaped implants represented 12% of implants. Smooth implants represented 47% of implants and textured implants represented 53% of implants.

For revision- reconstruction patients, the majority of implants (55%) were placed through a mastectomy or other scar, 33% were placed through an inframammary incision; 7% of implants were placed through a periareolar incision, and 2% were placed through a transaxillary incision. The placement was submuscular in 90% of implants and subglandular in 9% of implants. Round implants represented 87% of implants and shaped implants represented 13% of implants. Smooth implants represented approximately 39% of implants and textured implants represented 61% of implants.

The following two tables represent implant placement by cohort (Table 4) and breast implant style by cohort (Table 5).

TABLE 4. Breast Implant Placement by Cohort

Implant Placement	Primary Augmentation N=2,228	Revision Augmentation N=723	Primary Reconstruction N=420	Revision Reconstruction N=135
Submuscular	1,271 (57.0%)	438 (60.6%)	308 (73.3%)	121 (89.6%)
Subglandular	957 (43.0%)	285 (39.4%)	112 (26.7%)	12 (8.9%)
Other	0 (0%)	0 (0%)	0 (0%)	2 (1.5%)*

*Subcutaneous mastectomy bilateral

TABLE 5. Breast Implant Style by Cohort

Product Style	Primary Augmentation N=2,228	Revision Augmentation N=723	Primary Reconstruction N=420	Revision Reconstruction N=135
Round				
Style 10512 (Smooth)	47 (4.2%)	3 (0.8%)	8 (3.5%)	0 (0%)
Style 10521 (Smooth)	102 (9.1%)	12 (3.3%)	5 (2.2%)	0 (0%)
Style 20610 (Textured)	565 (50.7%)	127 (35.1%)	57 (24.9%)	8 (9.8%)
Style 20621 (Textured)	334 (30.0%)	139 (38.4%)	67 (29.3%)	26 (31.7%)
Shaped				
Style 20644 (Textured)	317 (28.4%)	91 (25.1%)	48 (21.0%)	14 (17.1%)
Style 20645 (Textured)	640 (57.4%)	217 (59.9%)	145 (63.3%)	57 (69.5%)
Style 20646 (Textured)	9 (0.8%)	9 (2.5%)	6 (2.6%)	5 (6.1%)
Style 20676 (Textured)	126 (11.3%)	42 (11.6%)	26 (11.4%)	6 (7.3%)

The Study is currently ongoing, and results available through 3 years are presented in this DFU. Sientra will periodically update this document as more information becomes available. Information on the safety and benefits of Sientra Implants is presented below and organized by indication.

RUPTURE INFORMATION ON SIENTRA'S IMPLANTS

Out of a total cohort of 3,506 implants in 1,788 patients, there have been three confirmed ruptures and six unconfirmed silent ruptures in eight patients through Year 3. These ruptures and suspected ruptures include two confirmed and five unconfirmed Implant ruptures occurring in six primary augmentation patients; one confirmed implant rupture occurring in one revision-augmentation patient; one unconfirmed implant rupture occurring in one primary reconstruction patient; and no ruptures occurring in revision-reconstruction patients. Based on analysis of the patients' data in the MRI cohort, the Kaplan-Meier calculated risk of rupture through three years is 2.0% on a by-patient basis (95% CI, 0.9%-4.1%). By cohort, the 3-year Kaplan-Meier risk of rupture was 2.5% (95% CI, 1.1%-5.5%) for primary augmentation patients and 2.8% (95% CI, 0.4%-18.1%) for primary reconstruction patients. There were no ruptures identified among the revision-augmentation and revision-reconstruction patients who underwent MRI through 3 years.

Sientra conducted a long-term rupture prevalence study in which MRI examinations were performed on 274 Implants in 140 women that assessed the rate of asymptomatic (or "silent") rupture in patients who received Silicone-Gel Breast Implants between 1990 and 2000. Overall, the long-term prevalence of rupture in the study was 7.7% by implant and 12.1% by patient, with a median implantation age of 14.4 years. In comparison, those implants with no evidence of rupture via MRI have a median duration of 10.2 years. These data support the low rate of rupture found in Sientra's Clinical Study and suggests that even over the long-term, over 14 years, Sientra's Silicone Gel Breast Implants have a relatively low rate of rupture. Additional information on rupture will be collected through Sientra's ongoing studies and from Sientra's postapproval studies.

PRIMARY AUGMENTATION AND REVISION-AUGMENTATION PATIENTS

The benefits and complications reported in the Study for primary and revision-augmentation patients are described below.

PATIENT ACCOUNTING AND FOLLOW-UP RATES

The Study enrolled 1,115 primary augmentation patients. Of the women expected to be seen at the 3-year follow-up visit, 80% were seen. The Study enrolled 362 revision-augmentation patients. Of the women expected to be seen at the 3-year follow-up visit, 79% were seen.

EFFECTIVENESS OUTCOMES

The benefits of Sientra Silicone Gel Breast Implants were determined by measuring bra size/chest circumference change and assessing patient satisfaction using patient-reported quality-of-life (QOL) outcomes, including the Short Form Health Survey (SF-36), the Rosenberg Self-Esteem Scale, and the Body Image Scale. The information was collected before implantation and at scheduled follow-up visits.

Primary Augmentation Patients
For primary augmentation patients, 91% of patients increased their bra cup size by at least one cup size. Over 81% of patients increased their bra cup size by one to two cups, while 10% gained more than two cup sizes. Of the patients, 6% achieved less than a 1-cup size increase. The change in bra cup size is unknown for the remaining 3% of patients.

The majority of primary augmentation patients were satisfied with their results. Other findings of the Study showed that over 90% of women felt their breast implants make them feel more feminine (94%) and more attractive (92%). In addition, the majority of women indicated that their breast implants made them feel better about themselves (85%).

For all eight subscales and at all time points, including Baseline, the mean SF-36 (Health Survey) QOL scores were significantly higher for the Study population compared to the general female population. For primary augmentation patients, comparisons of Baseline QOL scores to scores at Year 2 showed no clinically significant changes. There were a number of statistically significant decreases in the quality of life scales. However, effect sizes were small or very small and therefore the observed changes were judged not to be clinically relevant.

For primary augmentation patients, mean total self-esteem scores on the Rosenberg Self-Esteem Scale at Baseline and Year 2 remained above 25. Scores between 15 and 25 are considered to be within normal range, with higher scores indicating more positive feelings.

Mean scores on the Body Esteem Scale and subscales showed no clinically significant change from Baseline to Year 2 among women in the primary augmentation cohort. Scores were relatively high at baseline and remained high postoperatively.

Revision-Augmentation Patients
Bra cup size was not measured in revision-augmentation patients.

The majority of revision-augmentation patients in this Study were satisfied with their results. Another finding of the Study showed that most patients agreed that their breast implants make them feel more feminine (90%) and more attractive (89%). In addition, the majority of women indicated that their breast implants made them feel better about themselves (82%).

For all eight subscales and at all time points, including Baseline, the mean SF-36 (Health Survey) QOL scores were significantly higher for the Study population compared to the general female population. For revision-augmentation patients, comparison of baseline QOL scores to scores at Year 2 showed no clinically significant changes. There were a number of statistically significant decreases in the quality of life scales. However, effect sizes were small or very small and therefore the observed changes were judged not to be clinically relevant.

For revision-augmentation patients, mean total scores on the Rosenberg Self-Esteem Scale at Baseline and Year 2 remained above 25. Scores between 15 and 25 are considered to be within normal range, with higher scores indicating more positive feelings.

Mean scores on the Body Esteem Scale and subscales showed no clinically significant changes from Baseline to Year 2 among women in the revision-augmentation cohort. Scores were relatively high at baseline and remained high postoperatively.

SAFETY OUTCOMES

The safety of Sientra Implants was determined by assessing the incidence of complications, including device failures.

Primary Augmentation Patients
Table 6 describes the Kaplan-Meier risk of complications experienced for the primary augmentation patients in the Study.

TABLE 6. Kaplan-Meier Risk of Complications for Primary Augmentation Patients (N=1,115 Patients)

Key Complications	KM Risk	95% CI
Reoperation	12.6%	(10.7%, 14.8%)
Capsular Contracture (Baker Grade III/IV)	6.0%	(4.7%, 7.7%)
Implant Removal with Replacement	4.6%	(3.5%, 6.1%)
Implant Rupture (MRI cohort)	2.5%	(1.1%, 5.5%)
Implant Removal without Replacement	1.2%	(0.7%, 2.2%)
Other Complications Occurring at a KM Risk ≥1%[1,2]	**KM Risk**	**95% CI**
Nipple Sensation Changes	3.2%	(2.3%, 4.6%)

1. No ruptures were reported in the non-MRI cohort.
2. The following complications were reported at a risk rate of less than 1%: breast pain, hematoma, infection, hypertrophic/abnormal scarring, other complications, seroma/fluid accumulation, swelling, wrinkling/rippling, skin sensation changes, breast mass/cyst/lump, redness, delayed wound healing, implant visibility, bruising, implant extrusion, and upper pole fullness.
2. None of the following complications occurred: capsule calcification, implant palpability, irritation, lymphadenopathy, lymphedema, necrosis, nipple complications (not related to sensation), pneumothorax, and skin rash.

Revision-Augmentation Patients

Table 7 describes the Kaplan-Meier risk of complications for the revision-augmentation patients in the Study.

TABLE 7. Kaplan-Meier Risk of Complications for Revision-Augmentation Patients (N=362 Patients)

Key Complications	KM Risk	95% CI
Reoperation	20.3%	(16.3%, 25.0%)
Implant Removal with Replacement	8.7%	(6.1%, 12.4%)
Capsular Contracture (Baker Grade III/IV)	5.2%	(3.2%, 8.4%)
Implant Removal without Replacement	2.9%	(1.5%, 5.5%)
Implant Rupture (MRI cohort)[1]	--	--
Other Complications Occurring at a KM Risk ≥1%[2,3]	**KM Risk**	**95% CI**
Implant Malposition	3.2%	(1.7%, 5.9%)
Wrinkling/Rippling	2.4%	(1.2%, 4.8%)
Asymmetry	1.8%	(0.8%, 4.0%)
Nipple Sensation Changes	1.4%	(0.5%, 3.7%)
Infection	1.2%	(0.4%, 3.1%)
Seroma/Fluid Accumulation	1.2%	(0.5%, 3.3%)

1. No ruptures were reported in the MRI cohort. However, implant rupture was reported at a risk rate of 0.4% (0.1%, 2.9%) in the non-MRI cohort.
2. The following complications were reported at a risk rate of less than 1%: breast pain, hematoma, hypertrophic/abnormal scarring, other complications, ptosis, redness, swelling, delayed wound healing, implant extrusion, implant visibility, irritation, bruising, implant palpability, necrosis, and skin sensation changes.
3. None of the following complications occurred: breast mass/cyst/lump, capsule calcification, lymphadenopathy, lymphedema, nipple complications (not related to sensation), pneumothorax, skin rash, and upper pole fullness.

REASONS FOR REOPERATION

Primary Augmentation Patients

There were 149 reoperations performed in 127 primary augmentation patients through 3 years following implantation. Table 8 provides the primary reasons for reoperation. The most common reasons for reoperation through 3 years in these patients were capsular contracture (22%) and patient request for change in the style or size of the implant (20%).

TABLE 8. Main Reasons for Reoperation through 3 Years for Primary Augmentation Patients (N=149 Reoperations)

Reasons for Reoperation Through 3 Years[1]	n (%)
Capsular Contracture	33 (22.1%)
Patient Request for Size/Style Change	29 (19.5%)
Ptosis	18 (12.1%)
Hematoma/Seroma	17 (11.4%)
Implant Malposition	17 (11.4%)
Scarring/Hypertrophic Scarring	8 (5.4%)
Infection	6 (4.0%)
Asymmetry	5 (3.4%)
Wrinkling/Rippling	4 (2.7%)
Delayed Wound Healing	3 (2.0%)
Mass/Lump/Cyst	2 (1.3%)
Nipple-Related Complications	2 (1.3%)
Unknown	2 (1.3%)
Breast Cancer	1 (0.7%)
Upper Pole Fullness	1 (0.7%)
Pain	1 (0.7%)

1. Some reoperations were performed for multiple reasons; only the primary reason is provided in the table.

Revision-Augmentation Patients

There were 84 reoperations performed in 67 revision-augmentation patients through 3 years following implantation. Table 9 provides the main reasons for reoperation. In this population, the most common reasons for reoperation through 3 years were patient's desire for a change in the style or size of their implants (16%) and capsular contracture (16%).

TABLE 9. Main Reasons for Reoperation Through 3 Years for Revision-Augmentation Patients (N=84 Reoperations)

Reasons for Reoperation Through 3 Years[1]	n (%)
Patient Request for Size/Style Change	13 (15.5%)
Capsular Contracture	13 (15.5%)
Implant Malposition	11 (13.1%)
Wrinkling/Rippling	8 (9.5%)
Unknown	7 (8.3%)
Asymmetry	5 (6.0%)
Delayed Wound Healing	5 (6.0%)
Ptosis	5 (6.0%)
Hematoma/Seroma	4 (4.8%)
Infection	3 (3.6%)
Scarring/Hypertrophic Scarring	3 (3.6%)
Pain	2 (2.4%)
Breast Cancer	1 (1.2%)
Implant Extrusion	1 (1.2%)
Implant Palpability/Visibility	1 (1.2%)
Nipple-Related Complications	1 (1.2%)
Other[2]	1 (1.2%)

1. Some reoperations were performed for multiple reasons; only the primary reason is provided in the table.
2. Patient reported back pain from the weight of the Implants.

REASONS FOR IMPLANT REMOVAL

Primary Augmentation Patients

The main reasons for implant removal among primary augmentation patients through 3 years are provided in Table 10. There were 103 implants removed from 58 patients. Of these 103 implants, 82% were replaced. The most common reason for implant removal was the patient requesting a different implant style or size (56%).

TABLE 10. Main Reason for Implant Removal through 3 Years for Primary Augmentation Patients (N=103 Implant Removals)

Reason for Removal	n (%)
Patient Request for Size/Style Change	58 (56.3%)
Capsular Contracture	14 (13.6%)
Infection	7 (6.8%)
Implant Malposition	6 (5.8%)
Asymmetry	5 (4.9%)
Wrinkling/Rippling	4 (3.9%)
Unknown	3 (2.9%)
Hematoma/Seroma	2 (1.9%)
Ptosis	2 (1.9%)
Breast Cancer	1 (1.0%)
Delayed Wound Healing	1 (1.0%)

Revision-Augmentation Patients

The main reasons for implant removal among revision-augmentation patients through 3 years are provided in Table 11. There were 68 implants removed from 37 patients. Of these 68 implants, most were replaced (78%). The most common reason for implant removal was the patient requesting a different implant style or size (40%).

TABLE 11. Main Reason for Implant Removal through 3 Years for Revision-Augmentation Patients (N=68 Implant Removals)

Reason for Removal	n (%)
Patient Request for Size/Style Change	27 (39.7%)
Unknown	13 (19.1%)
Wrinkling/Rippling	8 (11.8%)
Asymmetry	4 (5.9%)
Capsular Contracture	3 (4.4%)
Implant Malposition	3 (4.4%)
Infection	3 (4.4%)
Other	3 (4.4%)
Hematoma/Seroma	2 (2.9%)
Breast Cancer	1 (1.5%)
Pain	1 (1.5%)

OTHER CLINICAL FINDINGS

The Study evaluated several long-term health effects that have been reported in breast implant patients. These include cancer, connective tissue disease (CTD), CTD signs and symptoms, lactation complications, reproduction complications, and suicide. These endpoints, along with others, are being further evaluated as part of the Study and a Sientra postapproval study of patients followed through 10 years.

Cancer
For primary augmentation patients, through 3 years, there have been two cases of breast cancer identified (0.2%) and no cases of fibrocystic breast disease. Diagnoses of any other (non-breast) cancers have been reported in 6 patients (0.5%) in the augmentation cohort through 3 years.

For revision-augmentation patients, through 3 years, there has been one case of breast cancer (0.3%) and no cases of fibrocystic breast disease. Diagnoses of any other (non-breast) cancers have been reported in 1 patient (0.3%) in the revision-augmentation cohort through 3 years.

There were no cases of BIA-ALCL in any of the patient cohorts.

Connective Tissue Disease
Among primary augmentation patients, through Year 3, two patients have reported confirmed CTDs: one case of fibromyalgia, and one case of rheumatoid arthritis. Among revision-augmentation patients, through Year 3, one patient has reported a confirmed CTD, which is fibromyalgia.

CTD Signs and Symptoms
In Sientra's Study, self-reported CTD signs and symptoms were collected. Compared to before having implants, for the pooled primary augmentation and revision-augmentation cohorts, significant increases were found in only 2 of the 13 CTD sign/symptom categories: *Pain and Fibromyalgia*, for which the statistical significance is driven by the prevalence of low back pain. These increases were not found to be related to simply getting older.

Conversely, compared to before having implants, significant decreases were found for 2 of the 13 CTD sign/symptom categories: Endocrine/Exocrine and Constitutional. For the category of Endocrine/Exocrine, the significance is driven by the low number of post-implantation reports of Hashimoto's Thyroiditis, while for the category of Constitutional the significance is driven by a decrease in Depression post-implantation.

The Sientra Study was not designed to evaluate cause-and-effect associations because there is no comparison group of women without implants, and because other contributing factors, such as medications and lifestyle/exercise, were not studied. Therefore, it cannot be determined whether or not these 2 increases and 2 decreases were due to the Implants.

However, your patients should be aware that there is a potential risk they may experience an increase in low back pain after receiving breast implants.

Lactation Complications
There were 150 primary augmentation patients experiencing at least one postoperative live birth; of these, 91% reported no difficulties with lactation after they received Sientra's Implants. Twelve of the 150 patients (8%) reported postoperative lactation difficulties, such as lack of milk production, mastitis or pain. In addition, one woman (0.7%) who had experienced preoperative lactation difficulties reported postoperative difficulties as well.

There were 39 revision-augmentation patients experiencing at least one postoperative live birth; of these, 95% reported no difficulties with lactation after they received Sientra's Implants. Two of the 39 patients (5%) reported postoperative lactation difficulties, such as lack of milk production or pain.

Reproduction Complications
Of the 1,115 patients in the primary augmentation cohort, 15 (1.3%) reported postoperative pregnancy difficulties through 3 years. Of the 362 patients in the revision-augmentation cohort, four (1.1%) reported postoperative pregnancy difficulties.

Suicide
There were no reports of suicide in primary augmentation or revision-augmentation patients in the Study through 3 years.

PRIMARY RECONSTRUCTION AND REVISION-RECONSTRUCTION PATIENTS

PATIENT ACCOUNTING AND FOLLOW-UP RATES

The Study enrolled 229 primary reconstruction patients, which includes 156 patients from the CORE clinical study and 73 patients from the Continued Access (CA) study. Of the women expected to be seen at the 3-year follow-up visit, 83% were seen.

The Study enrolled 82 revision-reconstruction patients, which includes 50 patients from the CORE clinical study and 32 patients from the CA study. Of the women expected to be seen at the 3-year follow-up visit, 76% were seen.

EFFECTIVENESS OUTCOMES

The benefits of Sientra Silicone Gel Breast Implants were determined by assessing patient satisfaction using patient-reported quality-of-life (QOL) outcomes, including the Short Form Health Survey (SF-36), the Rosenberg Self-Esteem Scale, and the Body Image Scale. The information was collected before implantation and at scheduled follow-up visits.

Primary Reconstruction Patients
The majority of primary reconstruction patients in this Study were satisfied with their results. The Study showed that most women felt their breast implants make them feel more feminine (79%) and more attractive (77%). In addition, the majority of women indicated that their breast implants made them feel better about themselves (72%).

For all eight subscales and at all time points, including Baseline, the mean SF-36 QOL scores were significantly higher for the Study population compared to the general female population. For primary reconstruction patients, comparison of baseline QOL scores to scores at Year 2 showed no clinically significant changes. There were a number of statistically significant decreases in the quality of life scales. However, effect sizes were small or very small and therefore the observed changes were judged not to be clinically relevant.

For primary reconstruction patients, mean total scores on the Rosenberg Self-Esteem Scale at Baseline and Year 2 remained above 25. Scores between 15 and 25 are considered to be within normal range, with higher scores indicating more positive feelings.

Mean scores for the Body Esteem Scale and subscales showed no clinically significant changes from Baseline to Year 2 among women in the primary reconstruction cohort. Scores were relatively high at baseline and remained high postoperatively.

Revision-Reconstruction Patients
The majority of revision-reconstruction patients in this Study were satisfied with their results. The Study showed that most women felt their breast implants made them feel more feminine (76%) and feel more attractive (76%). In addition, the majority of women indicated that their breast implants made them feel better about themselves (73%).

For all eight subscales and at all time points, including Baseline, the mean SF-36 QOL scores were higher for the Study population compared to the general female population. Comparisons of Baseline QOL scores to scores at Year 2 showed no clinically significant changes. There were a number of statistically significant decreases in the quality of life scales. However, effect sizes were small or very small and therefore the observed changes were judged not to be clinically relevant.

For revision-reconstruction patients, mean total scores on the Rosenberg Self-Esteem Scale at Baseline and Year 2 remained above 25. Scores between 15 and 25 are considered to be within normal range, with higher scores indicating more positive feelings.

Scores for the Body Esteem Scale and subscales showed no clinically significant changes from Baseline to Year 2 among women in the revision-reconstruction cohort. Scores were relatively high at baseline and remained high postoperatively.

SAFETY OUTCOMES

The safety of Sientra's Silicone Gel Breast Implants was determined by assessing the incidence of complications, including device failures.

Primary Reconstruction Patients
Table 12 describes the Kaplan-Meier risk of complications for the primary reconstruction patients in the Study.

TABLE 12. Kaplan-Meier Risk of Complications for Primary Reconstruction Patients Through 3 Years (N=229 Patients)

Key Complications	KM Risk	95% CI
Reoperation	34.9%	(28.9%, 41.8%)
Implant Removal with Replacement	19.1%	(14.3%, 25.3%)
Capsular Contracture (Baker Grade III/IV)	8.8%	(5.5%, 13.8%)
Implant Removal without Replacement	7.0%	(4.3%, 11.3%)
Implant Rupture (MRI cohort)[1]	2.8%	(0.4%, 18.1%)
Other Complications Occurring at a KM Risk ≥1%[1,2]	**KM Risk**	**95% CI**
Asymmetry	8.7%	(5.5%, 13.7%)
Infection	5.1%	(2.8%, 9.0%)
Redness	3.0%	(1.4%, 6.6%)
Implant Malposition	3.0%	(1.4%, 6.6%)
Hypertrophic/Abnormal Scarring	2.7%	(1.1%, 6.3%)
Breast Pain	2.6%	(1.1%, 6.1%)
Seroma/Fluid Accumulation	2.4%	(1.0%, 5.8%)
Nipple Sensation Changes	2.0%	(0.8%, 5.4%)
Ptosis	2.0%	(0.8%, 5.3%)
Swelling	2.0%	(0.7%, 5.2%)
Delayed Wound Healing	1.9%	(0.7%, 5.0%)
Implant Extrusion	1.5%	(0.5%, 4.5%)
Breast Mass/Cyst/Lump	1.0%	(0.3%, 4.0%)
Wrinkling/Rippling	1.1%	(0.3%, 4.3%)
Other Complications	1.1%	(0.3%, 4.4%)
Implant Visibility	1.0%	(0.3%, 4.1%)

1. No ruptures were reported in the non-MRI cohort.
2. The following complications were reported at a risk rate of less than 1%: bruising, hematoma, implant palpability, irritation, necrosis, skin rash, skin sensation changes and upper pole fullness.
3. None of the following complications occurred: capsule calcification, lymphadenopathy, lymphedema, nipple complications (not related to sensation), and pneumothorax.

Revision-Reconstruction Patients

Table 13 describes the Kaplan-Meier risk of complications for the revision-reconstruction patients in the Study.

TABLE 13. Kaplan-Meier Risk of Complications Reported for Revision-Reconstruction Patients Through 3 Years (N=82 Patients)

Key Complications	KM Risk	95% CI
Reoperation	42.5%	(32.0%, 54.8%)
Implant Removal with Replacement	23.2%	(14.8%, 35.1%)
Implant Removal without Replacement	10.3%	(5.0%, 20.6%)
Capsular Contracture (Baker Grade III/IV)	6.8%	(2.9%, 15.7%)
Implant Rupture (MRI cohort)[1]	--	--
Other Complications Occurring at a KM Risk ≥1%[2]	**KM Risk**	**95% CI**
Asymmetry	7.1%	(3.0%, 16.2%)
Implant Malposition	5.5%	(2.1%, 14.1%)
Breast Mass/Cyst/Lump	3.1%	(0.8%, 11.9%)
Hypertrophic/Abnormal Scarring	3.1%	(0.8%, 11.8%)
Wrinkling/Rippling	1.5%	(0.2%, 9.8%)
Breast Pain	1.4%	(0.2%, 9.3%)
Seroma/Fluid Accumulation	1.3%	(0.2%, 8.7%)
Infection	1.2%	(0.2%, 8.4%)

1. No ruptures were reported in the revision-reconstruction cohort (including both the MRI and the non-MRI cohorts).
2. None of the following complications occurred: bruising, capsule calcification, delayed wound healing, hematoma, implant extrusion, implant palpability, implant visibility, irritation, lymphadenopathy, lymphedema, necrosis, nipple complications (not related to sensation), nipple sensation changes, other complications, pneumothorax, ptosis, redness, skin rash, skin sensation changes, swelling and upper pole fullness.

REASONS FOR REOPERATION

Primary Reconstruction Patients

There were 85 reoperations performed in 74 primary reconstruction patients through 3 years following implantation. Table 14 provides the main reasons for reoperation. In this population, the most common reason for reoperation, through 3 years, was the patient's desire for a change in the style or size of the implant (25%).

TABLE 14. Main Reasons for Reoperation Through 3 Years for Primary Reconstruction Patients (N=85 Reoperations)

Reasons for Reoperation[1]	n (%)
Patient Request for Size/Style Change	21 (24.7%)
Asymmetry	16 (18.8%)
Infection	10 (11.8%)
Capsular Contracture	7 (8.2%)
Ptosis	5 (5.9%)
Implant Malposition	4 (4.7%)
Mass/Lump/Cyst	4 (4.7%)
Delayed Wound Healing	3 (3.5%)
Hematoma/Seroma	3 (3.5%)
Scarring/Hypertrophic Scarring	3 (3.5%)
Unknown	3 (3.5%)
Implant Extrusion	2 (2.4%)
Nipple-Related Complications	1 (1.2%)
Palpability/Visibility	1 (1.2%)
Skin Related	1 (1.2%)
Suspected Rupture	1 (1.2%)[2]

1. Some reoperations were performed for multiple reasons; only the primary reason is provided in the table.
2. This patient was confirmed non-ruptured via explant.

Revision-Reconstruction Patients

There were 38 reoperations performed in 31 revision-reconstruction patients through 3 years following implantation. Table 15 provides the main reasons for reoperation. In this population, the most common reasons for reoperation through 3 years were the patient's desire for a change in the style or size of her implants (26%) and asymmetry (24%).

TABLE 15. Main Reasons for Reoperation through 3 Years for Revision-Reconstruction Patients (N=38 Reoperations)

Reasons for Reoperation[1]	n (%)
Patient Request for Size/Style Change	10 (26.3%)
Asymmetry	9 (23.7%)
Capsular Contracture	6 (15.8%)
Implant Malposition	4 (10.5%)
Mass/Lump/Cyst	2 (5.3%)
Breast Cancer	1 (2.6%)
Hematoma/Seroma	1 (2.6%)
Infection	1 (2.6%)
Nipple-related Complications	1 (2.6%)
Pain	1 (2.6%)
Trauma	1 (2.6%)
Wrinkling/Rippling	1 (2.6%)

1. Some reoperations were performed for multiple reasons; only the primary reason is provided in the table.

REASONS FOR IMPLANT REMOVAL

Primary Reconstruction Patients

The main reasons for explantation among primary reconstruction patients through 3 years are provided in Table 16. There were 76 implants removed from 52 patients. Of these 76 implants, most were replaced (74%). The most common reason for implant removal was the patient requested an implant style or size change (45%).

TABLE 16. Main Reason for Implant Removal Through 3 Years for Primary Reconstruction Patients (N=76 Explants)

Reasons for Implant Removal	n (%)
Patient Request for Size/Style Change	34 (44.7%)
Asymmetry	14 (18.4%)
Infection	9 (11.8%)
Unknown	6 (7.9%)
Capsular Contracture	3 (3.9%)
Implant Malposition	3 (3.9%)
Implant Extrusion	2 (2.6%)
Scarring/Hypertrophic Scarring	2 (2.6%)
Delayed Wound Healing	1 (1.3%)
Hematoma/Seroma	1 (1.3%)
Suspected Rupture	1 (1.3%)[1]

1. This patient was confirmed non-ruptured via explant.

Revision-Reconstruction Patients

The main reasons for explantation among revision-reconstruction patients through 3 years are provided in Table 17. There were 30 implants removed from 22 patients. Of these 30 implants, most were replaced (73%). The most common reason for implant removal was the patient requested an implant style or size change (43%).

TABLE 17. Main Reason for Implant Removal through 3 Years for Revision-Reconstruction Patients (N=30 Explants)

Reasons for Implant Removal	n (%)
Patient Request for Size/Style Change	13 (43.3%)
Asymmetry	5 (16.7%)
Implant Malposition	3 (10.0%)
Pain	2 (6.7%)
Trauma	2 (6.7%)
Breast Cancer	1 (3.3%)
Capsular Contracture	1 (3.3%)
Hematoma/Seroma	1 (3.3%)
Infection	1 (3.3%)
Wrinkling/Rippling	1 (3.3%)

OTHER CLINICAL FINDINGS

The Study evaluated several long-term health effects that had been previously reported in breast implant patients. These include rupture, cancer, connective tissue disease (CTD), CTD signs and symptoms, lactation complications, reproduction complications and suicide.

Rupture

Out of a total cohort of 3,506 implants in 1,788 patients, there have been three confirmed ruptures and six unconfirmed silent ruptures in eight patients through Year 3. These ruptures and suspected ruptures include one unconfirmed implant rupture occurring in one primary reconstruction patient; and no ruptures occurring in revision-reconstruction patients. Based on analysis of the patients' data in the MRI cohort, the 3-year Kaplan-Meier risk of rupture was 2.8% (95% CI, 0.4%-18.1%) for primary reconstruction patients. There were no ruptures identified among the revision-reconstruction patients who underwent MRI through 3 years.

Cancer

There have been no new cases of breast cancer or fibrocystic breast disease identified in primary reconstruction patients through 3 years. Diagnoses of any other (non-breast) cancers have been reported in 7 patients (3%) in the primary reconstruction cohort through 3 years. The other types of cancer include lung, ovarian, skin, and metastatic cancers.

Two revision-reconstruction patients reported breast cancer through 3 years in the Study. This represents a risk of 3.6%. There were no cases of fibrocystic disease among revision-reconstruction patients through 3 years. One case of metastatic cancer (liver and spine) was reported in the revision-reconstruction cohort. This represents a rate of 1.2%.

There were no cases of BIA-ALCL in any of the patient cohorts.

Connective Tissue Disease (CTD)

No primary reconstruction or revision-reconstruction patients have been diagnosed with a CTD in the 3 years after receiving implants.

CTD Signs and Symptoms

In Sientra's Study, numerous self-reported CTD signs and symptoms were collected. Compared to before having implants, for the pooled primary reconstruction and revision-reconstruction cohorts, a significant increase was found in only 1 of the 13 sign/symptom categories: *EENT*, for which the statistical significance is driven by reports of dry eyes. This increase was not found to be related to simply getting older.

The Sientra Study was not designed to evaluate cause-and-effect associations because there is no comparison group of women without implants, and because other contributing factors, such as medications and lifestyle/exercise, were not studied. Therefore, it cannot be determined whether or not this 1 increase was due to the implants.

However, your patients should be aware that they may experience an increase in dry eyes after receiving breast implants.

Lactation Complications

There were 16 primary reconstruction patients who delivered a baby after reconstruction with Study Implants. None of these patients reported difficulties with lactation after they received the Implants.

There was one revision-reconstruction patient who delivered a baby after reconstruction with Study Implants; this patient reported no problems with lactation.

Reproduction Complications
Of the 229 patients in the primary reconstruction cohort, 2 (0.9%) reported postoperative difficulties through 3 years. Of the 82 patients in the revision-reconstruction cohort, none (0%) had postoperative difficulties.

Suicide
There were no reports of suicide in primary reconstruction or revision-reconstruction patients in the Study through 3 years.

National Breast Implant Registry
In collaboration with the U.S. Food and Drug Administration (FDA) and breast implant device manufacturers, 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 prospective, non-interventional, population-based, outcomes and safety surveillance registry and quality improvement initiative. The NBIR collects clinical, procedural and outcomes data at the time of operation and any subsequent reoperations. Data collection is anticipated to continue as long as breast implants are being manufactured. The NBIR is currently only open to physicians practicing in the United States.

If your patient agrees to participate in the NBIR, you can use the registry to submit device tracking data to the breast implant manufacturers by completing the NBIR case report form (CRF). If your patient does not want to participate in the NBIR, you cannot use the registry for device tracking and will need to use the paper device tracking form that is in the implant box.

To learn more about the NBIR go to the following link: https://www.thepsf.org/documents/Research/Registries/NBIR/nbir-physician-faq.PDF

INSTRUCTIONS FOR USE

Back-up Implants should be available during the procedure.

Do not use more than one implant per breast.

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

PREOPERATIVE PATIENT PROCEDURES

Sientra relies on the surgeon to know and follow proper surgical procedures when implanting, explanting or performing revising surgery with Sientra's Implants. Proper surgical planning, such as allowance for adequate tissue coverage, implant placement, incision site, implant size, shape, style, and texture, should be made preoperatively. The surgeon should take into consideration the contraindications, warnings and precautions described in this document, as well as the patient's medical history, desires, and expectations, and physical condition.

INSTRUCTIONS FOR OPENING AND INSPECTING THE STERILE PACKAGE

1. Examine the implant's sealed outer box before entering the surgical area to verify package integrity. **Do not utilize any implant with packaging that appears to be damaged in any way.**
2. Open the outer box and remove the interior double blister packaging.
3. Separate the product accessories, such as the *Directions for Use*, the Device Identification Card, Breast Implant Tracking Form, and the adhesive labels.
4. Attach the adhesive labels with the product data to the patient's operative report and patient Device Identification (ID) Card. Make sure to provide the Device ID card to the patient after surgery.
5. Open the outer blister package to gain access to the inner sterile blister packaging, taking care not to contaminate the inner sterile blister packaging by touching it to the outside of the outer blister.
6. Open the sterile inner blister package being careful to avoid contact with dust, lint and talc, and place the implant onto the surgical tray.

Do not implant any device that

- Appears to have particulate contamination, damage, or loss of shell integrity,
- Appears to have leaks or nicks, or
- Is damaged or contaminated.

The Sientra Implants are sterilized by dry heat. Do not re-sterilize the product.

INTRAOPERATIVE CONSIDERATIONS

Take note of the following intraoperative considerations:

- Have a spare Implant available during the surgical procedure and all follow-up procedures, revisions and capsulotomies.
- The periumbilical approach has not been studied in Sientra's Study and should not be used for a variety of reasons, including potential damage to the implant shell.
- To avoid damaging the device, ensure that the incision is sufficiently large to facilitate insertion without excessive manipulation and handling of the device.

Do not use lubricants to facilitate placement.

Use extreme care to avoid damaging the breast implant with sharp surgical instruments such as needles and scalpels, or with cautery devices or blunt instruments such as clamps or forceps, or by over handling and manipulation during introduction into the surgical pocket.

Do not use excessive force during breast implant placement.

Please refer to the *Warnings and Precautions* sections in this document for additional information about intraoperative considerations.

POSTOPERATIVE CONSIDERATIONS

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 damage to the implant from sharp instruments.

MANAGING A RUPTURED IMPLANT

Physicians should recommend implant removal to their patients if a rupture is confirmed.

In the event of rupture of a breast implant, 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 Sientra. In the event of breast implant rupture, contact Sientra at (888) 708-0808.

ADDITIONAL PRODUCT-SPECIFIC INFORMATION

RETURNED MERCHANDISE POLICY

Product returns should be processed through a Sientra Sales Representative or through the Sientra Customer Experience Team at (888) 708-0808. All package seals must be intact to be eligible for return.

EXPLANTED DEVICE RETURNS AND REPORTING

Explanted devices must be returned to Sientra and the reason for explantation must be provided. All explanted devices must be returned in a Sientra Explant Return Kit. Please contact the Sientra Customer Experience Team at (888) 708-0808 for a Sientra Explant Return Kit and instructions.

PRODUCT REPLACEMENT POLICY AND LIMITED WARRANTIES

The Sientra Platinum20™ Limited Warranty and Lifetime Product Replacement Program provides lifetime replacement and limited financial reimbursement in the event of shell leakage or breakage resulting in implant rupture, or complications of capsular contracture Baker Grade III/IV, double capsule, late forming seromas and BIA-ALCL, subject to certain conditions as discussed in the Sientra Platinum20 Limited Warranty literature. Our standard Platinum20 Limited Warranty program applies to every Sientra breast implant recipient subject to

their participation in Sientra's Device Tracking program and to the conditions discussed in the Sientra Platinum20 Limited Warranty literature. For more information, please contact Sientra Customer Service at (888) 708-0808.

PRODUCT ORDERING

To order directly in the U.S.A. or for product information, please contact Sientra's Customer Experience Team at (888) 708-0808.

ACCESS TO ELECTRONIC INFORMATION

The *Patient Educational Brochures*, *Patient Decision Checklist*, and *Device Tracking Form* can be found on Sientra's website at www.Sientra.com. The electronic version of this DFU can also be found on Sientra's website.

REPORTING PROBLEMS

The U.S. Food and Drug Administration requires healthcare providers to report serious injuries involving medical devices (defined as those that need medical or surgical intervention to prevent permanent damage) to the manufacturer and/or to FDA. In addition, injuries or complications can be voluntarily reported directly by the patient to FDA's MedWatch.

If you have a patient who has experienced one or more serious problems related to her breast implants, you are encouraged to report the serious problem(s) to FDA through the MedWatch voluntary reporting system for her. Examples of serious problems include disability, hospitalization, harm to offspring, and medical or surgical intervention to prevent lasting damage.

You are also required to report any product problem or serious adverse effect to Sientra. Deaths must be reported to Sientra and FDA. You can report by telephone to 1-800-FDA-1088 (1-800-332-1088); by FAX, use Form 3500 to 1-800-FDA-0178 (1-800-332-0178); electronically at http://www.fda.gov/medwatch/index.html; or by mail to MedWatch Food and Drug Administration, HFZ-2 Fishers Lane, Rockville, MD 20857-9787. Keep a copy of the completed MedWatch form for your records.

This information reported to MedWatch is entered into databases to be used to follow safety trends and to determine whether further follow up of any potential safety issues related to the device is needed.

DEVICE MANUFACTURER

Sientra's Silicone Gel Breast Implants are manufactured for and sold by:

Sientra, Inc.
PO Box 1490, Santa Barbara, CA 93116-1490
U.S. Toll-Free Phone: (888) 708-0808
Phone: (805) 562-3500
Fax: (805) 562-8401
www.sientra.com

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