

Core Gel Study of the Safety and Effectiveness of Mentor Round Low Bleed Silicone Gel-filled Mammary Prostheses in Patients who are undergoing Primary Breast Augmentation, Primary Breast Reconstruction or Revision



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Table of Contents

	Synopsis	i
1.0	Introduction	1
2.0	Objectives	1
3.0	Risks and Benefits of the Procedure	2
4.0	Study Design	8
5.0	Device Description	9
6.0	Patient Population	9
7.0	Patient Enrollment	10
8.0	Patient Inclusion Criteria	10
9.0	Patient Exclusion Criteria	11
10.0	Study Evaluations	11
10.1	Baseline Visit	11
10.2	Operative Day	13
10.3	Follow-up Visits	13
10.4	MRI Scan	14
10.5	Missed Visits	14
10.6	Interim Visits	15
10.7	Secondary Procedures/Reimplantation	15
10.8	Final Evaluation	15
10.9	Discontinuation from Study	15
10.10	Conditions for Modifying/Terminating Study	15
11.0	Returned Devices	16
12.0	Monitoring Procedures	16
13.0	Medical Director	17
14.0	Adverse Event Reporting	18
15.0	Serious Unanticipated Adverse Device Effects	18
16.0	Data Collection & Management	19
17.0	Statistical Consideration	19
17.1	Safety Endpoints	19
17.2	Effectiveness Endpoints	19
17.3	Sample Size	20
17.4	Statistical Analysis	23
18.0	Investigator Selection	24
19.0	IRB Approval	24

20.0	Informed Consent	24
21.0	Confidentiality	25
22.0	Investigator Compliance	25
23.0	Data Submission Requirements	26
24.0	References	29

ATTACHMENTS

ATTACHMENT 1	STUDY VISIT SCHEDULE
ATTACHMENT 2	PRODUCT INSERT DATA SHEET
ATTACHMENT 3	INFORMED CONSENT
ATTACHMENT 4	BAKER CLASSIFICATION SCALE
ATTACHMENT 5	QUALITY OF LIFE QUESTIONNAIRES
ATTACHMENT 6	INVESTIGATOR AGREEMENT
ATTACHMENT 7	MRI PROTOCOL
ATTACHMENT 8	STUDY DEFINITIONS
ATTACHMENT 9	STUDY DEVICES
ATTACHMENT 10	CASE REPORT FORMS
ATTACHMENT 11	CORE GEL RETRIEVAL PLAN

Synopsis - Core Gel Study of Mentor Round Low-Bleed Silicone Gel-filled Prostheses

Objective: Demonstrate safety and effectiveness of Mentor's Round Low-Bleed Silicone Gel-filled Mammary Prostheses in women who are undergoing primary augmentation, primary reconstruction, or revision.

Design:

- Multicenter
- Non-masked, open label
- Two year data submitted to FDA as part of PMA
- Following FDA clearance, follow up data collected: Rheumatic Disease Diagnosis, QoLs, silent rupture, and Adverse Events

Population:

- Total subject population: 1000
 - Augmentation: 550
 - Reconstruction: 250
 - Revision: 200
- Total number of investigational sites: up to 40
 - Augmentation: 20
 - Reconstruction: up to 20
 - Revision done by both Augmentation and Reconstruction sites
- Maximum number of subjects per site: 15% of cohort
 - Augmentation: 83
 - Reconstruction: 38
 - Revision: 30
- MRI Substudy: \approx 11 patients/site

Study Device: Mentor Round Low Bleed Gel-filled Mammary Prostheses, both Siltex and smooth surface

Inclusion Criteria:

- Subject is Genetic female and at least 18 years old
- As defined in Section 6.0, a candidate for:
 - Primary breast augmentation (for post-lactational mammary involution or general breast enlargement)
 - Primary breast reconstruction (for cancer, trauma, surgical loss of breast or congenital deformity)
 - Revision surgery (previous augmentation or reconstruction with silicone-filled or saline-filled implants)
- Signs the Informed Consent
- Agrees to follow the procedures for explant analysis.
- Agrees to comply with follow-up procedures, including returning for all follow-up visits

Exclusion Criteria:

- Subject is pregnant
- Has nursed a child within three months of study enrollment.
- Been implanted with any silicone implant other than breast implants
- Confirmed diagnosis of rheumatic disease
- Currently has a condition that could compromise or complicate wound healing (except reconstruction patients).
- Patient in Augmentation cohort and has diagnosis of active cancer of any type.

Synopsis - Core Gel Study (continued)

Exclusion Criteria (continued):

- Infection or abscess anywhere in the body.
- Demonstrates tissue characteristics which are clinically incompatible with implant (e.g. tissue damage resulting from radiation, inadequate tissue, or compromised vascularity).
- Possesses any condition, or is under treatment for any condition which, in the opinion of the investigator and/or consulting physicians(s), may constitute an unwarranted surgical risk.
- Anatomic or physiologic abnormality which could lead to significant postoperative adverse events.
- Demonstrates characteristics that are unrealistic/unreasonable with the risks involved with the surgical procedure.
- Premalignant breast disease without a subcutaneous mastectomy.
- Untreated or inappropriately treated breast malignancy, without mastectomy.
- Implanted metal or metal devices, history of claustrophobia or other condition that would make a MRI scan prohibitive.

Study Evaluation Schedule Summary:

Data Collected	Timeframe				
	Baseline	Operative	6 Months	12 & 24 Months	3 – 10 Years*
Inclusion/Exclusion	X				
Subject Consent	X				
Medical/Breast History	X				
Breast Measurements	X		X	X	X
Mammography (if performed)	X		X	X	X
Quality of Life**	X			X	X
Nipple/Breast Sensitivity Assessment	X		X	X	X
Capsular Contracture			X	X	X
Rheumatology Assessment	X			X	X
Surgical Information		X			
MRI Scan ^θ				X	X
Adverse Events***		X	X	X	X

* At 3, 4, 5, 6, 7, 8, 9, and 10 years.

** Rosenberg Self Esteem Scale, SF-36, Body Esteem Scale, Tennessee Self-Concept Scale, FLIC (Cancer patients only)

^θ MRI scan done on a subset of 405 subjects at 1, 2, 4, 6, 8, and 10 years

*** Including secondary procedures and reimplantations

Safety Endpoint: Incidence, severity, method of resolution, and duration for all adverse events on a per implant and per patient basis

Effectiveness Endpoints:

Primary: Changes in chest circumference and bra and cup size (may not be applicable to reconstruction subjects)

Secondary: Changes in Quality of Life results

1.0 INTRODUCTION

Silicone gel-filled breast implants were introduced in the early sixties and were in wide-scale distribution by the time the Medical Device Amendments to the Food Drug and Cosmetic Act was passed in 1976. In 1983, gel-filled breast implants were designated as Class III devices requiring premarket approval. In May 1990, the Food and Drug Administration (FDA) published a proposed request (515(b)) for Premarket Approval Applications (PMA) and in April 1991 published the final request. This final publication put manufacturers of gel-filled breast implants on notice that for continued marketing of gel-filled breast implants, a PMA was due to FDA in 90 days from the final publication date.

A premarket approval (PMA) for the Mentor gel-filled breast implants was filed with the FDA in July 1991. At the FDA General and Plastic Surgery Advisory Committee meeting in November 1991, the committee recommended the submission of additional information to establish the safety and effectiveness of gel-filled breast implants.

In January 1992, the FDA Commissioner announced a voluntary moratorium of the sale of gel-filled breast implants to allow the advisory panel time to assess additional information. In April 1992, the moratorium was lifted but only for reconstruction and revision patients. Every patient implanted had to be part of an adjunct study, and had to be offered participation in a registry of gel-filled breast implant patients. In order to be implanted with gel-filled implants for augmentation, women had to be enrolled in a core clinical study.

This protocol describes the study design procedures, population, variables and analyses for the evaluation of safety and effectiveness of Mentor silicone gel-filled smooth and textured breast implants for breast augmentation, reconstruction, and revision

2.0 OBJECTIVES

The objective of this study is to determine the safety and effectiveness of the smooth and textured surface Mentor Round Low-Bleed Silicone Gel-filled Mammary Protheses in women who are undergoing primary breast augmentation, primary breast reconstruction or revision.

Safety will be determined by:

- The incidence, severity, method of resolution, and duration for all adverse events on a per implant and a per patient basis

Effectiveness will be determined by:

- Primary - changes in chest circumference and bra and cup size
- Secondary - changes in quality of life questionnaire results

3.0 RISKS AND BENEFITS OF THE PROCEDURE

Patient Notification

The implanting physician must insure that the patient clearly understands the potential risks and benefits of the procedure and agrees that the potential benefits associated with the procedure outweigh the risks. The risks of the procedure are outlined in the Product Insert Data Sheet (Attachment 2) and the Patient Informed Consent (Attachment 3). The physician must discuss these with the patient.

3.1 Benefits of the Procedure

Breast augmentation surgery is an elective cosmetic surgery designed to provide both physical and psychological benefits. The physical benefits include increased options and choices in selection and fit of clothing. Psychologically, the procedure may improve the woman's self-esteem, sense of body image and quality of life. The primary motivation of women seeking this procedure is to enhance appearance by enlarging the breast, usually associated with an improvement in shape. The anatomic variances perceived as a deformity by the woman include: size smaller than her perceived ideal, ptosis, asymmetry, and post partum or post lactation involution. For the vast majority of patients, this represents a single focus concern in an otherwise satisfactory life environment.

Breast reconstruction is usually performed to restore the breast after surgical loss of one or both breasts due to cancer, severe cystic disease as well as congenital deformity. Women have reported that breast reconstruction with mammary implants has been an aid in their recovery from breast cancer and has reduced emotional stress by helping to return their bodies to a more natural appearance, as opposed to not having reconstructive surgery or wearing an external prosthesis.

The effectiveness of the implants will be measured by assessing the increase in the size of the breast and by administering validated quality of life questionnaires.

3.2 Surgical Risks of the Procedure

All surgical procedures have a small risk of complication inherent to the surgery itself and to anesthesia. These risks include:

3.2.1 Infection: (severe infection on rare occasions results in Toxic Shock Syndrome or TSS). An infection can result from any surgery and produce swelling, tenderness, pain and fever. Almost all infections appear within a few days of the operation but may appear at any time after surgery.

3.2.2 Hematoma: formation (a collection of blood in the surgical area)

3.2.3 Seroma: (fluid accumulation around the implant which may or may not require removal). The body will absorb both areas of fluid accumulation (seromas) and small hematomas, but large ones may have to be drained surgically to permit proper healing.

3.2.4 Scarring: Any incision in the skin will leave a scar that is permanent. While surgeons will use plastic surgical techniques to make this as inconspicuous as possible, some patients have a skin quality that results in more conspicuous scars no matter how the incision is repaired.

3.2.5 Anesthetics: There are risks from anesthetics as well.

3.3 Risks Specific to Breast Implants

Risks specific to breast implants include:

3.3.1 Capsular Contracture

Capsular contracture is the most common side effect of breast implants. To accept the implant, a surgical pocket behind the breast is made somewhat larger than the implant itself. Normally a healing scar forms an envelope around the implant, which, on occasion, will shrink sufficiently to squeeze the implant, producing varying degrees of firmness. The implant can feel hard, be painful and/or distorted. This can occur soon after surgery or years later and may be unilateral, bilateral or asymmetric. Surgical release or excision of the scar is often successful but recurrence is not uncommon. The cause of the contracture phenomenon is poorly understood and is probably related to an idiosyncratic response to the presence of normal, benign skin bacteria, *Staphylococcus epidermidis*. In the past, closed disruption of the scar by squeezing the breast was common, but this is rarely practiced today. This practice will be prohibited in this study. Capsular contracture is graded in severity on a scale of I to IV by Baker classification. (Attachment 4).

Calcification of the capsule can also occur. This is usually associated with Grade IV contracture. Calcification is a phenomenon that is occasionally seen with long term scarring especially if there is irritation such as tight burn scars that cross joints. Calcified capsules may require removal if the patient wishes relief from her contracture but otherwise seem to be harmless. Small foci of calcification are commonly seen anywhere in the breast parenchyma. They can usually be identified as benign by the radiologist but on occasion may require biopsy to rule out a malignancy. These do not seem to be more common in the augmented patient. (Please see section 3.3.6 for further information)

3.3.2 Rupture of the Implant

Breast implants may not last a lifetime. While the silicone material itself has not been shown to biodegrade, the shell may rupture due to wear and tear, or direct injury. If the implant shell is ruptured, the escaping gel is usually contained by the scar envelope in the surgical pocket (intracapsular) and may be undetectable except by Magnetic Resonance Imaging (silent rupture) which is about 85% effective in detecting rupture. If the scar envelope is torn, the gel can be driven into the local tissue planes and breast tissue (extracapsular). Most of the escaped gel remains in the immediate environment of the breast but on rare occasions it has been reported to migrate down the arm, into nerve sheaths or into the abdominal wall. The free silicone may cause lumps called granulomas to form in the breast or other tissues where the silicone has migrated. Some studies indicate that silicone may escape the capsule in 10-20% of rupture cases.⁴⁷

Ultrasound, mammography and physical examination may also diagnose these ruptures which have escaped the scar envelope.

The rate at which silicone gel-filled implants rupture is uncertain. However, using different methods of detection, published studies suggest a rupture rate between 5 and 51 percent.^{47a} A study of screening mammograms suggested that 5% of asymptomatic women had experienced "silent rupture" of their implants. Mammography is of limited value in detecting implant rupture.

The mammogram readings of rupture were not confirmed by surgical removal of the implant. Robinson et al. studied 300 women who had their implants for 1 to 25 years and had their implants removed for a variety of reasons.^{47b} They found visible signs of ruptures in 51 percent of the women studied. Severe silicone leakage -- silicone outside the implant without visible tears or holes -- was seen in another 20 percent, without visible tears or holes. Robinson et al. also noted that the probability of rupture increases as the implant ages and recommended removal of all gel-filled implants preferably before 8 years of implantation.

Rupture should be suspected if there is a change in character of the device such as a new, persistent unilateral burning sensation or a change in softness, texture or shape of the implant. Because of the silent nature of most ruptures and the difficulty of diagnosis without surgical exploration, the true incidence is unknown. Caution should be used when comparing expected or actual rupture rates of current devices to historical incidences, especially when, as is often the case, the brand, vintage and type of device is unknown. Explantation and/or replacement may be indicated if the implant fails, especially if it is seen in the breast parenchyma as it could be confused with or mask a tumor.

Causes of implant rupture include, but are not limited to: damage from surgical instruments, intraoperative or postoperative trauma, excessive stresses or manipulations as may occur during daily routines such as vigorous exercise, contact athletics, routine manual massage, intimate physical contact and from compression required during mammography.

Most of the reported cases occurred in the more fragile, thinner shell devices implanted in the late 1970's. Current products have thicker and stronger shells and more cohesive gel contents. Caution should be used when comparing expected or actual rupture rates of current devices to historical incidences, especially when, as is often the case, the brand, vintage and type of device is unknown.

3.3.3 Gel Bleed

The gel in an implant consists of a three-dimensional crosslinked structure that constitutes about 15 % of the total volume. The interstices are filled with silicone oil. This oil is similar to the materials available in many products including anti-gas medication, available without prescription for infants and adults. The shell of the implant is slightly permeable to the oils. Depending on the age, brand, chemical characteristics and environmental mechanics of a given device, varying small amounts of the oil diffuses or "bleeds" through the shell.

Some amount diffuses into the scar envelope where it can be picked up by macrophages, the probable mechanism by which it is transported into regional lymph nodes. The oil has been detected in the breast and surrounding subcutaneous tissues in amounts diminishing with distance. It is assumed that minute amounts of silicone from all ingested and injected sources are distributed throughout the body. Because silicone is hydrophobic, it is unlikely to be transported by any mechanism other than macrophage migration or local diffusion. There is no evidence to suggest that the gel contents have any different metabolic effect on the body than the solid silicone envelope.³⁷

3.3.4 Changes in Nipple and Breast Sensation/Breast Pain

Any surgery of the breast can result in undersensitive or oversensitive nipple-areolar complexes and/or undermined areas of breast skin. These changes can vary in degree and may be temporary or permanent. Changes in nipple/breast sensation may, on occasion, affect sexual response or comfort while nursing. These changes are believed to be a result of nerve damage from the surgery and not the presence of the implant itself.

Most women undergoing augmentation or reconstruction with a mammary prosthesis will experience some breast and/or chest pain postoperatively. While this pain normally subsides in most women as they heal after surgery, it can become a chronic problem in other women. Chronic pain can be associated with hematoma, migration, infection, and implants that are too large or capsular contracture. Sudden severe pain may be associated with implant rupture.

3.3.5 Interference with Mammography in Detection of Cancer

As silicone is opaque to x-rays, an implant may interfere with the early detection of cancer by mammography as it may obscure part of the breast.

Newer techniques of breast compression improve the amount of breast that can be visualized. Alternatively, most surgeons feel that the device may improve the detection of tumors by palpation. While of considerable theoretical concern, delayed detection due strictly to the presence of an implant has not been reported. Women at high risk of developing breast cancer should consider getting implants with caution. Since the breast is compressed during mammography, it is possible for the implant to rupture, but this is rare and should not deter a woman from regular, routine mammographic screening. Before the mammography exam, women should inform the technologist that they have implants.

3.3.6 Calcium Deposits

Calcium deposits are seen occasionally in old scars anywhere in the body and this is true of the implant capsule. This usually does not occur until years after implant surgery. Benign calcifications are also commonly seen on mammography in otherwise normal breast parenchyma even in breasts that have never been operated on. These benign calcium deposits usually have a different x-ray appearance than the calcifications that signal a malignancy. An expert radiologist can usually determine if a calcium spot is benign or malignant but occasionally a biopsy may be necessary to rule out malignancy.

There is no evidence that these deposits occur more or less frequently in women with implants than those who have not received implants.

After many years, some patients may develop a thin layer of calcium in the scar capsule that surrounds the implant. This is almost always associated with capsular contracture but otherwise causes no known problem. (Please see capsular contracture section 3.3.1 for information on risk of developing calcium deposits with implants)

3.3.7 Delayed Wound Healing

In some cases, the incision site fails to heal normally.

3.3.8 Extrusion

Unstable or compromised tissue covering and/or interruption of wound healing may result in extrusion, which is when the breast implant comes through the skin.

3.3.9 Necrosis

Necrosis is the formation of dead tissue around the implant. This may prevent wound healing and require surgical correction and/or implant removal. Permanent scar deformity may occur following necrosis. Factors associated with increased necrosis include infection, use of steroids in the surgical pocket, smoking, chemotherapy/radiation, and excessive heat or cold therapy.

3.3.10 Breast Tissue Atrophy/Chest Wall Deformity

The pressure of the breast implant may cause the breast tissue to thin and shrink. This can occur while implants are still in place or following implant removal without replacement.

3.3.11 Dissatisfaction with Cosmetic Results

Visible and/or palpable wrinkles in an implant are related to the thinness of the overlying tissue cover, the degree of capsular contracture and the texturing of the implant shell surface. Traditional smooth walled gel devices rarely demonstrate wrinkles.

Surgical error, preexisting asymmetry or deformity, keloid formation of the incisional scar, vagaries of time, weight gain or loss, pregnancy and nursing can all contribute to an immediate or late poor aesthetic result. With time most breasts, with or without implants, become ptotic to some degree. Asymmetry is usually related to the inability to totally correct for pre-existing disparity between the two breasts. It can also be attributed to surgical error, asymmetric contracture, or rupture of the implant.

Excessive buildup of collagen at the incision site during the healing process causes some patients to develop scars of cosmetic concern. Keloid scars, which do not respond well to treatment, often extend beyond the edges of the original scars and can continue to enlarge over time. Hypertrophic scars are generally confined to the original site and respond well to scar revision treatment, which may include steroid injections to break down the collagen or surgery to revise the position, direction or line of the scar.

3.3.12 Granulomas

It is possible for a granuloma to form around a tiny amount of silicone. Although these lumps are non-cancerous, they can be difficult to distinguish from cancerous lumps without being removed (biopsied) and examined.

3.3.13 Resurgery

Women should understand there is a high chance they will need to have additional surgery at some point to replace or remove the implant. Also, problems such as rupture, capsular contracture, infection, shifting, and calcium deposits can require removal of the implants. Many women decide to have the implants replaced, but some women do not. Those who do not may have cosmetically unacceptable dimpling and/or puckering of the breast following removal of the implant.

3.4 Unknown Risks

The issue of the possible relationship between silicone (and other implantable materials) and various diseases has been the subject of significant scientific debate. Concerns include immunological and neurological disorders, carcinogenicity and connective tissue disorders.

3.4.1 Connective Tissue Disease

The term Connective Tissue Disorder has been used to describe a variety of symptoms thought to be related to silicone breast implants. Some cases of these disorders have been reported in women with breast implants, and some of these women have reported a reduction in symptoms after their implants have been removed. Several studies have explored whether a possible link exists between silicone breast implants and connective tissue disorders or other immunological diseases.^{7,8,9,10,11,12,13,14,38,39}

3.4.2 Neurological Disorders

Co-incident neurological problems such as multiple sclerosis and amyotrophic lateral sclerosis (ALS) have occurred in a small number of breast implant patients.^{15,16,17,18,19,20}

3.4.3 Cancer

Case reports in the medical literature have associated tumors with the presence of silicone breast implants. Several studies have been conducted to determine the carcinogenic risk of breast implants and no evidence of increased risk of cancer has been demonstrated.^{21,22,23,24,25,26,27,40,41,42} Continuing assessment of both known and possible carcinogenic risks associated with breast implant surgery is ongoing.

3.4.4 Birth Defects

No credible reports on birth defects or other reproductive effects in humans associated with implantation of silicone mammary prostheses of any type have been identified in the literature. Recent studies^{28,29,30} provide further evidence that silicone materials used in mammary prosthesis do not cause adverse reproductive effects in experimental animals.

3.4.5 Breast Feeding

Although any breast surgery, including breast implantation, could theoretically interfere with the adequacy of the woman's milk supply, many women with breast implants have nursed their babies successfully. It is known that any breast surgery such as breast biopsy can affect the quantity of milk produced.

In recent years, the question has been raised regarding the potential transfer of silicone into the breast milk of women with silicone breast prostheses and possible effects on the health of breast fed children.^{31,32}

However, more recent studies have provided strong evidence of the lack of association between silicone breast implants and adverse effects in breast fed children.^{33,34}

3.5 Minimization of Risks

Mentor will select investigators qualified by experience and training to participate in the clinical study. Mentor will require each investigator to submit a copy of his/her curriculum vitae and medical license (see Section 18.0).

Mentor will insure that all investigator's conduct the clinical study properly by:

- following the requirements of the protocol and IDE regulations, including supervising the use of the implants, which are outlined in the Investigator Agreement (Attachment 6)
- protect the rights, safety and welfare of subjects and to ensure that an informed consent is obtained before they begin study participation (Section 20.0).
- insuring that the investigator will obtain IRB approval prior to enrolling patients (Section 19.0).
- Mentor will conduct periodic audits of patient logs, device accountability records, source documentation and case report forms to insure that the protocol is strictly followed. (Section 12.1.)

The investigator may be disqualified from the study by failing to comply with any of the requirements of the protocol or any FDA regulations. (Section 22.0)

4.0 STUDY DESIGN

This trial is designed as an open label, multi-center study, with each patient as her own control. There will be three treatment groups:

- Primary augmentation
- Primary reconstruction
- Revision

Mentor will submit the PMA after completion of two-years of patient follow-up. All patients will continue to make follow-up visits at 3, 4, 5, 6, 7, 8, 9 and 10 years post surgery. The study will include 10 years of long term follow-up data for each patient

There will be up to 40 centers with a total of 1000 patients. Up to 20 centers will be designated to recruit the primary augmentation cohort, and up to 20 will be designated to recruit the primary reconstruction cohort. Both groups will recruit the revision cohort.

- Ratio of siltex surface to smooth surface will be determined by market demand.
- No more than 15% of the total number of patients in a cohort may be enrolled at one center (see table below)
- Assuming the proportion of patients lost to follow-up is no greater than 20%, there should be at least 800 evaluable subjects at the end of 2 years.

All patients at each study center who meet inclusion and exclusion criteria will be offered participation in this study. The study will be open to augmentation, reconstruction, and revision patients. It is expected that no more than 550 of the women will be breast augmentation patients, no less than 250 of the women will be reconstruction patients, and no less than 200 will be revision patients.

Total Number of Patients in Each Cohort

Cohort	Study Total	Maximum/Site (15% of Total)
Augmentation (20 sites)	550	83
Reconstruction (20 sites)	250	38
Revision (From both Augmentation and Reconstruction Cohort sites)	200	30

Depending on the rate of enrollment, all sites may not be able to enroll the allocated number of patients.

All patients enrolled in the study will participate in the Mentor patient registry. This registry of confidential information has been established for Mentor's other breast implant studies, including the Adjunct Study. The registry will enable Mentor to inform patients of safety related information in a timely manner.

5.0 DEVICE DESCRIPTION

Two types of Mentor Round Low-Bleed Silicone Gel-filled Mammary Prostheses will be used in the study: the Siltex textured surface device and the smooth surface device. Each implant is a silicone elastomer mammary device that is supplied individually packaged in a doubled wrapped packaging system, sterile, and non-pyrogenic. Each device consists of a silicone shell encasing a silicone gel filler material with a patch on the posterior side of the device. The basic smooth device shell consists of a crosslinked phenyl silicone elastomer layer sandwiched in between crosslinked methyl silicone elastomer layers. The phenyl layer acts as a barrier to slow the diffusion of any gel filler materials through the shell. The Siltex textured shell consists of a smooth shell to which is bonded an additional layer of silicone with a textured pattern imprinted into its surface.

The Siltex shell is intended to provide a disruptive surface for connective tissue ingrowth. The gel filler is a crosslinked silicone polymer. All study devices will be manufactured from SiTech/NuSil silicone materials.

See Attachment 9 for a list of the sizes and catalogue numbers of study devices.

6.0 PATIENT POPULATION

The study population will consist of women aged 18 or over who are undergoing primary breast augmentation, primary breast reconstruction or revision.

Augmentation

The Augmentation cohort will include patients who have post-lactational mammary involution or wish general breast enlargement.

Reconstruction

The Reconstruction cohort will include patients with loss of breast due to mastectomy or with deformities secondary to disease, malignancy, trauma, and congenital deformity.

Congenital deformities will include deformities of the breast itself as well as skeletal abnormalities reflected in breast deformity or asymmetry.

Asymmetry is one or more of the following conditions:

- One cup size difference in breast size.
- The need to differentially pad one bra cup to match the opposite breast size.
- Asymmetry due to chest wall deformity such as scoliosis or other deformities of the thoracic cage and/or associated visible differences in shoulder height that can make one breast appear to be at a different height than the other.

Revision

Patients in this cohort will have had previous breast augmentation or reconstruction with silicone or saline filled implants.

Both Augmentation and Reconstruction sites will enroll patients into the Revision cohort. Augmentation cohort sites will enroll augmentation revision patients only, while Reconstruction Cohort sites will enroll reconstruction revision patients.

Revision Cohort patients will not have been previously enrolled in the Core Gel Study. If a patient was previously enrolled in the Core Gel study as an Augmentation or Reconstruction patient, they will remain in that cohort throughout the study, even if they have a reoperation or revision.

7.0 PATIENT ENROLLMENT

A total of 1000 patients will be enrolled at up to 40 centers. A minimum of 800 assessable patients is required to be evaluable at two years. Patients will be considered enrolled in the study after implantation. Enrollment is targeted to be complete in approximately eight months.

8.0 PATIENT INCLUSION CRITERIA

Study subjects will be allowed to enter the study if the following inclusion criteria are met:

- Patient is genetic female, 18 years of age or older.
- As defined in Section 6.0, a candidate for:
 - Primary breast augmentation (for post-lactational mammary involution or general breast enlargement)
 - Primary breast reconstruction (for cancer, trauma, surgical loss of breast or congenital deformity)
 - Revision surgery (previous augmentation or reconstruction with silicone-filled or saline-filled implants)
- Signs the Informed Consent.
- Agrees to follow the procedures for explant analysis.
- Agrees to comply with follow-up procedures, including returning for all follow-up visits.

9.0 PATIENT EXCLUSION CRITERIA

Study subjects will not be allowed to enter the study if they have any of the following exclusion criteria:

- Patient is pregnant.
- Has nursed a child within three months of study enrollment.
- Been implanted with any silicone implant other than breast implants (e.g. silicone artificial joints or facial implants).
- Confirmed diagnosis of the following rheumatic diseases or syndromes: SLE, Sjogren's syndrome, scleroderma, polymyositis, or any connective tissue disorder, rheumatoid arthritis, crystalline arthritis, infectious arthritis, spondyarthropathies, any other inflammatory arthritis, osteoarthritis, fibromyalgia, or chronic fatigue syndrome.
- Currently has a condition that could compromise or complicate wound healing (except reconstruction patients).
- Patient in Augmentation cohort and has diagnosis of active cancer of any type.
- Infection or abscess anywhere in the body.
- Demonstrates tissue characteristics which are clinically incompatible with implant (e.g. tissue damage resulting from radiation, inadequate tissue, or compromised vascularity).
- Possesses any condition, or is under treatment for any condition which, in the opinion of the investigator and/or consulting physicians(s), may constitute an unwarranted surgical risk.
- Anatomic or physiologic abnormality which could lead to significant postoperative adverse events.
- Demonstrates characteristics that are unrealistic/unreasonable with the risks involved with the surgical procedure.
- Premalignant breast disease without a subcutaneous mastectomy.
- Untreated or inappropriately treated breast malignancy, without mastectomy.

- Implanted metal or metal devices, history of claustrophobia or other condition that would make a MRI scan prohibitive.

10.0 STUDY EVALUATIONS

All assessments for each patient will be performed by the investigator and/or coordinator according to the "Study Visit Schedule" (Attachment 1). Section 10 describes all study evaluations that will be monitored during study visits.

The study is composed of the following study intervals:

- Baseline (within 30 days of surgery)
- Operative Day
- Follow-up visits (6 months, 1, 2, 3, 4, 5, 6, 7, 8, 9 and 10 years post surgery)
- MRI scan at 1, 2, 4, 6, 8,10 years post surgery (subgroup only)

10.1 Baseline (within 30 days of surgery)

Patients who meet the inclusion criteria for the study will have the informed consent explained to them. The patients will also be given an information booklet that explains eligibility requirements, the history of breast implants, surgical procedures, requirements of study participation and the risks and benefits of implant surgery.

If the patient agrees to participate in the study and signs the informed consent, the **Baseline** case report form will be completed. The following assessments will be recorded on this form:

- Baseline nipple and breast sensitivity
- Baseline breast size will be measured by both bra and cup size and the chest/bust circumference
- Medical history and physical exam
- Breast History (includes previous surgeries, radiation and chemotherapy treatments)
- Rheumatic Disease Diagnosis Questionnaire
- Concomitant medications
- Psychometric testing with the following Quality of Life Questionnaires will be administered to all patients at this visit (Attachment 6):
 1. Rosenberg Self Esteem Scale
 2. Body Esteem Scale
 3. Tennessee Self Concept Scale
 4. SF-36 Health Survey
 5. The Manitoba Cancer Treatment and Research Foundation Functional Living Index (FLIC) (cancer patients only)

The Rheumatic Disease Diagnosis Questionnaire captures rheumatic disease, symptom and rheumatic physical exam data. In addition, the Investigator is asked, in his or her medical opinion, do the patient's symptom(s) warrant a rheumatological exam? If yes, a rheumatological confirmation is required. This information ensures that "confirmed" rheumatologic conditions are captured.

Examination by mammography is not required in this study. However, if the patient undergoes a mammogram within 30 days of surgery, the results will be recorded under "Mammography Results" on the Baseline form.

10.2 Operative day

The operative procedure is to take place no more than 30 days following the screening visit. The investigator will record the type and size of the prosthesis along with the catalogue numbers and lot numbers, the type of surgery and anesthesia, and other procedure related information on the **Operative Report** case report form. In addition, the lot numbers, catalogue numbers and demographic information will be recorded on the **Patient Registry** form. Any adverse events, which occur during the procedure, will be recorded on the **Adverse Event Report form**.

10.3 Postoperative Follow-up Evaluation Visits

Follow-up evaluations will take place at 6 months and 1, 2, 3, 4, 5, 6, 7, 8, 9 and 10 years after surgery.

Any unscheduled postoperative visits will also be recorded and submitted to Mentor on the **Interim Visit** form. Adverse events will be documented upon occurrence.

6 Month Postoperative Follow-up Visit

At the 6 month postoperative follow-up visit, the following procedures and evaluations will be performed and recorded on the **6 Month Visit** case report form:

- Nipple and breast sensitivity assessment
- Breast measurements
- Capsular contracture assessment
- Concomitant medication
- Adverse Event Evaluation

Postoperative Follow-up Visits at 1, 2, 3, 4, 5, 6, 7, 8, 9 and 10 years

At each scheduled follow-up visit, the following procedures and evaluations will be performed and recorded on the appropriate case report forms for that visit (i.e. **1 Year Visit, 2 Year Visit, etc**):

- Nipple and breast sensitivity assessment
- Breast measurements
- Capsular contracture assessment
- Concomittant medication
- Quality of Life Questionnaires (at 1, 2, 4, 6, 8, and 10 year visits only)
- Adverse Event Evaluation
- MRI scan on subset of patients (at 1, 2, 4, 6, 8, and 10 year visits only)
- Rheumatic Disease Diagnosis Questionnaire

The Rheumatic Disease Diagnosis Questionnaire captures rheumatic disease, symptom and rheumatic physical exam data. In addition, the Investigator is asked, in his or her medical opinion, do the patient's symptom(s) warrant a rheumatological exam? If yes, a rheumatological confirmation is required. This information ensures that "confirmed" rheumatologic conditions are captured.

Examination by mammography is not required in this study. However, if the patient undergoes a mammogram while enrolled in the study, the results will be recorded under "Mammography Results" on the postoperative follow up forms.

10.4 MRI Scan

In addition to the examinations listed above, a subset of all patients will undergo a MRI scan at 1, 2, 4, 6, 8 and 10 years post surgery to detect silent rupture (Attachment 7). Patients will be informed at study entry that they possibly may be randomized to undergo the MRI scans.

MRI centers in close proximity to the study sites will be identified. The participating MRI facility will be required to have at least a 1.5 Tesla magnet with a dedicated breast coil. Adequacy of the MRI site will be judged at the time the site is selected.

As a silent rupture rate of 5% is anticipated ⁸, 405 patients will undergo a MRI scan. After all patients have been enrolled, these patients will be randomly selected so that of the 405 patients, 55% will be from the augmentation cohort, 25% will be from the reconstruction cohort and 20% will be from the revision cohort.

All patients, whether or not they are randomized to undergo MRI scans, will be directed to see their physician whenever the patient believes a rupture has occurred. These patients will undergo a MRI scan. The scans will be sent to a central reading center to be read by an independent breast MRI radiologist. This radiologist will be blinded to the patient name and site.

The results will be recorded on the MRI Silicone Breast Evaluation Data Sheet (Attachment 7) and entered into the study database.

10.5 Missed Visits

Every effort will be made to assure that study subjects comply with the study visit schedule listed in Attachment 1. If a patient misses her scheduled appointment, she will be contacted and another appointment will be made.

If she misses two consecutive follow-up visits, the subject will be withdrawn from the study and considered lost to follow-up. Subject withdrawal will be documented by completing the **End of Study** form. The patient will be in compliance with the visit schedule if she is evaluated within the following visit windows relative to the date of surgery:

- 6-month: \pm 4 weeks
- 1-year: \pm 6 weeks
- 2 years: \pm 8 weeks

- 3, 4, 5, 6, 7, 8, 9 and 10 years: \pm 4 months

10.6 Interim Visits

If any complication or other problem arises outside the window of scheduled study visits, the patient may be seen at an interim appointment. The information gathered at the interim visit will be entered on the **Interim Visit** case report form. This case report form is a duplicate of the scheduled visit case report forms. If any adverse events are noted during an interim visit, that information should be recorded on the **Adverse Event Report**. The information should include type of complication, date of onset, therapy or other action (if any), date of resolution, severity, and relatedness to the device.

10.7 Secondary Procedures/Reimplantation

For each instance of explantation, revision, re-implantation or other secondary procedures, the date and reason will be collected and the **Secondary Procedures Report** case report form will be completed. If a new study device is implanted, the **Reimplantation Report** will be completed. **Any adverse events related to reoperative procedure, as well as the surgery itself, will be recorded on the Adverse Events Report.**

10.8 Final Evaluation Visit

The final evaluation will be made at the ten year follow-up examination. In the event that a woman withdraws from the study, every effort will be made by Mentor to have her evaluated before withdrawal with a final evaluation visit. The last study visit will be documented by completing the **End of Study** case report form.

10.9 Discontinuation from Study

In the event that a patient indicates her intention to withdraw from the study, the reason for the withdrawal will be recorded on the **End of Study** case report form. If possible, she will be requested to come in for a final evaluation visit. The final evaluation visit will include breast measurements, adverse event report and psychometric testing. If the patient moves from the implanting surgeon's area an investigator appropriate to her new location will be requested to assume follow-up.

10.10 Conditions for Modifying or Terminating the Study

Any modification of the study parameters will be made only with the approval of the Sponsor and Investigator(s). Protocol amendments that impact on patient safety or the science of the study must be approved by the IRB responsible for the review and approval of the study (Investigator responsibility). The changes must also be submitted to the FDA for review (Sponsor responsibility) as required by the Code of Federal Regulations (CFR 21 Part 812.35).

If the Investigator or Sponsor discovers conditions during the study which indicate it should be terminated, a recommendation to terminate the study may be made after consultation between the Sponsor and Investigator. The study will be terminated under an appropriate schedule designed so as not to jeopardize the health of any patient (CFR 21 Part 812.46)

11.0 RETURNED DEVICES

All explanted breast prostheses should be returned to Mentor Product Evaluation. The investigator should contact Mentor Clinical Programs Department by phone at 800-525-0245 extension 6411. Arrangements will be made for the site to be sent an explant kit, which includes a "Field Experience Report". In addition, the "Secondary Procedures" and "Reimplantation Report" case report form should be completed and sent to Mentor Clinical Programs.

Upon receipt of the implant, Mentor Product Evaluation will examine the returned implant in order to evaluate the complaint. Product Evaluation will conduct a comprehensive investigation including visual and physical testing of the explanted device to try and determine the cause for the complaint, in accordance with established procedures and protocols. The Core Gel Retrieval Protocol will be utilized to evaluate explanted devices specifically from this study (Attachment 11). Each complaint will be evaluated for MDR determination per the requirements of "MDR Reporting Guidance for Breast Implants."

12.0 SITE MONITORING PROCEDURES

Effective and efficient technical and medical communication between Mentor and the investigators will, in part, be accomplished by clinical monitoring procedures. These monitoring procedures will ensure that the Sponsor knows about each investigator's participation in enough detail to assess adherence to the clinical study protocol. In addition, the following monitoring procedures will allow the Sponsor to secure investigator compliance with:

1. The signed investigator agreement,
2. The investigational plan,
3. Adherence to applicable FDA regulations, and
4. Any conditions of approval imposed by the IRB or FDA.

If it is determined that the investigator violates any of the above provisions, the Sponsor will promptly secure compliance or cease breast implant shipments.

In addition, the non-compliant investigator will return the breast implants immediately without jeopardizing the rights, safety, or welfare of a subject (21 CFR 812.46 [a]). The following study monitors, along with other qualified persons, will undergo product training and be properly oriented in monitoring procedures prior to study initiation:

- Emily Hergenreter, CRA at (805) 879-6412
- Carolyn Offutt, Sr. CRA at (805) 879-6411

12.1 Clinical Site Monitoring Procedures

Monitoring procedures will, at minimum, consist of the following:

12.1.1 Initial on-site visit. The Clinical Monitor will review the terms of the protocol with the investigator and confirm the investigator's access to facilities required to conduct the study. The Clinical Monitor will answer any questions the investigator may have concerning the protocol, case report form completion and submission, investigator responsibilities, device tracking, source documentation and regulatory requirements.

Investigators will be provided with a Study Reference Manual, which outlines all study procedures. No devices will be sent to a site until the initial on-site visit has been satisfactorily completed and IRB approval has been received by the sponsor.

12.1.2 In-house review of data. The Sponsor will conduct an ongoing in-house review of data submitted by investigators, with checks for accuracy and completeness. Investigators will be contacted and asked to submit any missing information or clarify any questionable data. As data are entered into the database, edit checks will be performed and data queries will be resolved.

12.1.3 Periodic follow-up with investigators. The Clinical Monitor will periodically contact investigators, either by written correspondence or by telephone, to assess the current status of the clinical study.

Notes from telephone conversations and copies of written correspondence between the Clinical Monitor and the investigators will be maintained in the study file. Periodic visits to clinical sites may also be required to assure that the facilities and personnel being used continue to be acceptable; the clinical protocol terms are being followed, and accurate, complete, and current records are being maintained and submitted to Mentor on a timely basis.

12.1.4 Final on-site visit (Study Completion). The Clinical Monitor will visit each investigator at the end of the 10 year follow-up period for all implanted patients. The purpose of this visit will be to discuss the study ending with the investigator and complete closeout activities.

A final review of study records will be completed to ensure the presence of all relevant documents maintained by the investigator, including IRB approvals, informed consent (original and revisions), protocol, correspondence, monitoring logs, study procedure manuals, device tracking logs, medical records, correspondence, source documents and study agreements. Patient files will be reviewed to ensure all case report forms have been submitted, all data queries have been resolved and all adverse events have been reported. The investigator will be informed of requirements for records retention, follow-up procedures and IRB notification of study closure. The Clinical Monitor will review the inventory log and confirm the disposition of all prostheses that have been shipped to the site. If applicable, all devices and device-related equipment should be returned to Mentor

13.0 MEDICAL DIRECTOR

Mentor has designated Dr. Gary Brody as Medical Director for this study:

Garry Brody, M.D.
1450 San Pablo St., Suite 2000
Los Angeles, CA. 90033
(323) 442-6462

The Medical Director is responsible for providing professional guidance to the Sponsor on matters of a clinical nature. Dr. Brody will review all serious adverse events. He will also review any clinical submissions to be sent to FDA, such as Annual Reports. Dr. Brody will be available throughout this study to provide clinical expertise to the investigators participating in this study.

In addition to Dr. Brody, other qualified individuals may be consulted as necessary. For example, Rebecca Anderson, Ph.D. will provide guidance on effectiveness endpoints, relating to Quality of Life questionnaires, and Dr. David Gorczyca has developed the MRI substudy protocol and will be the MRI masked reviewer.

Rebecca Anderson, Ph.D.
Medical College of Wisconsin
Clinics of Froedtert
9200 West Wisconsin Avenue
Milwaukee, Wisconsin 53226
(414) 454-5464

David Gorczyca, MD
9037 Eagle Hills Drive
Las Vegas, NV 89134
(702) 731-8060

14.0 ADVERSE EVENTS

An adverse event is defined as any undesirable clinical occurrence in a subject whether it is considered to be device related or not (Clinical Investigation of Medical Devices for Human Subjects - EN 540:1993). During the procedure and at each follow-up visit, the investigator will record all adverse events, device related or non-device related, on the **Adverse Event Report** form.

Adverse events associated with breast implants and the surgical procedure include, but are not limited to, Baker III or Baker IV capsular contracture, hematoma, seroma, delayed wound healing, necrosis, breast pain, new diagnosis of breast cancer, lactation difficulties, ptosis, irritation/inflammation, asymmetry, hypertrophic scarring, lymphadenopathy, extrusion, wrinkling, calcification, nipple/breast sensitivity change, silicone granuloma, fluid accumulation, infection and any secondary surgical procedures.

Implant change due to cosmetic dissatisfaction is considered an adverse event. Staged reconstruction, nipple tattooing or nipple reconstruction are not considered adverse events and will be recorded on the Secondary Procedures Report.

15.0 SERIOUS UNANTICIPATED ADVERSE DEVICE EFFECTS

Serious, unanticipated adverse events, are defined as any adverse occurrence, side effect, injury, toxicity, or sensitivity reaction that reasonably suggests adverse events from the implant which involve death, life threatening conditions or permanent impairment of body function which have not been addressed in the product literature or which has been addressed, but is occurring with unexpected severity or frequency. These include rheumatologic conditions.

Any unanticipated adverse event associated with the device or procedure which occur during the clinical study must be reported to the Mentor Clinical Monitor by telephone and the associated Adverse Event Report will be faxed to Mentor within 72 hours of report of occurrence. Information required to be reported includes the time the reaction occurred or was first observed, a complete description of the event, its severity, probable cause, the patient's condition, and any actions or treatment taken by the investigator.

An Investigator or Sponsor who determines that an unanticipated adverse device effect presents an unreasonable risk to subjects shall terminate all or a portion of investigations as soon as possible so as not to jeopardize the health of any patient.

Termination shall occur not later than 5 working days after the sponsor makes this determination and not later than 15 working days after the sponsor first receives notice of effect. Resumption of terminated studies can occur only with IRB and FDA approval.

16.0 DATA COLLECTION AND MANAGEMENT

The clinical data described in this protocol will be gathered using the specified case report forms (Attachment 10). Data will be recorded on appropriate forms for each visit. Data entry will be by double entry with cross validation of entries.

16.1 Data Validation

Discrepancies in the database will be queried and reconciled. Range checks of the continuous variables will be performed and non-valid entry errors for categorical variables will be resolved. Errors emanating from the CRF will be traced to source documentation for resolution. A random sample of records will be 100% audited for accuracy.

17.0 STATISTICAL CONSIDERATIONS

17.1 Safety Study Endpoints

Safety endpoints include point prevalence on a per patient and per device basis of the following:

- Rates of occurrence of all adverse events, including infection, seroma, capsular contracture by Baker classification, rupture, explant, and silent rupture.
- Time to occurrence of the complication.

17.2 Effectiveness Study Endpoints

Effectiveness endpoints include:

- Change in breast size measured by both bra and cup size and the chest/bust circumference. These measurements were chosen because they have proven effective as a measure of breast size change in other studies and they are universally accepted measures.
- Patient satisfaction measured by the following validated quality of life questionnaires:
 1. Rosenberg Self Esteem Scale
 2. Body Esteem Scale
 3. SF-36 Health Survey
 4. Tennessee Self Concept Scale
 5. The Manitoba Cancer Treatment and research Foundation Functional Living Index (FLIC) (cancer patients only)

The Rosenberg Self Esteem was chosen because self-esteem is an important quality of life measure particularly as it relates to body image change. Global measures of self-esteem will be obtained from the Tennessee Self-Concept Scale.

Global quality of life measures will be assessed by the use of the SF-36 Health Survey, which provides a measure of both physical and mental health. The Body Esteem Scale provides a measure of general body esteem, sexual attractiveness, weight concern, and physical condition.

17.3 Sample Size

The estimation of a sample size is usually based on either statistical estimation or hypothesis testing. Since the aim of the Core Gel Study is to estimate the rate of complication in breast implant patients, the sample size for this study will be based on the statistical estimation of a complication rate within a specified level of precision. This is accomplished by making the half-width of a confidence interval about the mean an acceptable value. Since this study is intended to estimate complication rates, the estimation process will focus on limiting the upper confidence limit.

This is accomplished by using one-sided confidence limits. One-sided 95% confidence limits will be used for these sample size determinations.

To obtain a sample size estimate, the exact binomial distribution is used, in iterative fashion, to find the sample size that provides the acceptable level of precision for the rate being estimated. The computations provided below were performed using StatXact, Version 4.01.

In the Adjunct Study, the rate of infection from reconstruction patients who returned for their one-year examination ranges between 3.7% to 4.5% depending on the subgroup chosen for evaluation. The rate for reconstruction patients who only returned for their one-year visit was 4.5%. Assuming that the infection rate for augmentation and reconstruction patients will be similar, the 4.5% rate is chosen for the infection sample size calculations given in the table below.

Total Sample Size to Estimate the Rate of Infection within the Stated Level of Precision

Sample Size	Rate (%)	Exact One-sided Upper Confidence Limit (%)	Interval Half-Width (%)
150	4.7	8.6	3.9
175	4.6	8.1	3.5
200	4.5	7.7	3.2
250	4.4	7.2	2.8
300	4.7	7.2	2.5
350	4.6	6.9	2.3

A sample size of 350 yields an upper 95% one-sided confidence limit of 6.9 with an interval half-width of 2.3.

The current rate of capsular contracture (Baker Class III or IV) for reconstruction patients in the Adjunct Study ranges from 9.4% to 15.7% depending on the subgroup used for estimation.

As above, assuming that the rate for augmentation and reconstruction patients will be similar to that for reconstruction patients in the Adjunct study, the rate of 15.7% for reconstruction patients who had both one and three-year examinations will be used in the table below will be used to estimate the sample size for augmentation and reconstruction patient rate of capsular contracture.

Total Sample Size to Estimate the Rate of Capsular Contracture of Baker Class III or IV within the Stated Level of Precision

Sample Size	Rate(%)	Exact One-sided Upper Confidence Limit (%)	Interval Half-Width (%)
175	15.4	20.6	5.2
200	15.5	20.3	4.8
225	15.6	20.1	4.5

A sample of 225 subjects will provide an estimate of 15.7% with a precision of 4.5%.

Rupture is a long-term and somewhat rare event. The current rate of rupture for reconstruction patients in the Adjunct Study ranges from 1.2% to 2.0% depending on the subgroup used for estimation with one to two years of implant experience. For the purposes of this sample size evaluation, the 2.0% value from reconstruction patients who had both one and three-year examinations will be used in table below.

Total Sample Size to Estimate the Rate of Rupture within the Stated Level of Precision

Sample Size	Rate (%)	Exact One-sided Upper Confidence Limit (%)	Interval Half-Width (%)
400	2.0	3.6	1.6
450	2.0	3.5	1.5
500	2.0	3.4	1.4
550	2.0	3.3	1.3
600	2.0	3.2	1.2
650	2.0	3.2	1.2
700	2.0	3.1	1.1
750	2.0	3.1	1.1
800	2.0	3.0	1.0

A sample of 800 patients will provide an estimate of a 2% rupture rate with a precision of 1.0. This sample size and precision is consistent with that discussed in the January 11, 1996 draft guidance for breast implant manufacturers. Thus a sample size of 800 patients, followed for two years, will be used in the Core Gel Study. Assuming that the withdrawal rate will be 20% or less, the total number of patients to be enrolled into the study is $800/0.8=1000$ of which at least 25% will be primary reconstruction patients. The estimate of the point prevalence of infection with 800 or more patients at two years will be 4.8% with an upper one-sided 95% confidence limit of 6.2% (precision of 1.6%). Further, the estimate of the point prevalence of capsular contracture of Baker Class III or IV is 15.8% with an upper limit of 18.0% (precision of 2.2%).

The rate of silent rupture has been reported to be between 5.0% to 10.0%. The sample size calculations given in the table below provide estimates of sample size for three rates, 5.0%, 7.5%, and 10.0%. Based on estimates of rupture incidence in FDA sponsored trials, a rate of 5% was chosen.⁴⁸

Total Sample Size to Estimate the Rate of Silent Rupture within the Stated Level of Precision

Sample Size	Rate(%)	Exact One-sided Upper Confidence Limit (%)	Interval Half-Width (%)
250	5.2	8.1	2.9
300	5.0	7.6	2.6
324	4.9	7.4	2.5
175	7.4	11.6	4.2
200	7.5	11.3	3.8
210	7.6	11.3	3.7

Sample Size	Rate(%)	Exact One-sided Upper Confidence Limit (%)	Interval Half-Width (%)
100	10.0	16.4	6.4
125	10.4	16.0	5.6
150	10.0	15.0	5.0

If the silent rupture rate is 5%, at 2 years, then a sample size of 324 yields an estimate of 4.9% with an upper 95% one-sided confidence limit of 7.4 and an interval half-width of 2.5%. If the silent rupture rate is 7.5%, then a sample of 210 subjects produces an estimate of 7.6% with an upper 95% one-sided confidence limit of 11.3 and an interval half-width of 3.7.

If the silent rupture rate were 10%, then a sample of 150 patients would yield a rate of 10% with a 95% one-sided upper confidence limit of 15% and an interval half-width of 5%. To be conservative a rate of 5% was chosen by Mentor, resulting in an MRI sample size of 324. To assure a sample size of 324 at two-years, $324/0.8=405$ patients must be enrolled in the MRI substudy.

The recent October 1999 draft guidance from FDA indicated that follow-up for ten years should be considered in the sample size computations. The draft guidance provides an example of the follow-up of 500 patients though ten years with about 25% from reconstruction and a possible lost-to-follow-up rate of 40%. The sample size obtained in the Core Gel study using the same assumptions is 600 subjects at ten years and would yield the following estimates and one-sided upper 95% limits of the rate of rupture.

Estimates and Rate of Rupture within the Stated Level of Precision for 600 Subjects Followed for Ten Years

Sample Size	Rate(%)	Exact One-sided Upper Confidence Limit (%)	Interval Half-Width (%)
600	50.0	53.4	3.4
600	40.0	43.4	3.4
600	30.0	33.2	3.2
600	25.0	28.1	3.1
600	20.0	22.9	2.9
600	15.0	17.6	2.6
600	10.0	12.3	2.3
600	5.0	6.7	1.7
600	2.0	3.2	1.2

These estimates are clearly in the range of those discussed in the draft guidance and should support the rupture rates at ten years.

The distribution recommended at ten years in the draft guidance is about 25% reconstruction and 75% augmentation. This relative ratio may not be possible to achieve at ten years. While a minimum of 25% of the patients are reconstruction patients at the start of the study, the agency should clearly understand that these are cancer patients whose survival to ten years may be severely compromised.

It is unlikely that the survival of these patients will be similar to that of an otherwise healthy augmentation population. Even with no loss to follow-up, a proportion of the reconstruction group will have only a 50% five-year survival. Even in the most favorable circumstances, the five-year survival is likely to be around 90%. It is unlikely that any sponsor can meet this suggested target.

17.4 Statistical Analysis

The appropriate statistic for demographic and prognostic variables gathered at baseline will be estimated with associated 95% confidence intervals. A statistical justification for pooling across study sites will be done. Deviations will be noted and those variables found to be dissimilar between the two groups will be considered covariates in further analyses.

For continuous variables such as patient age, the analysis will be done by a two-sample t-test or a Wilcoxon signed rank test. For categorical variables such as nodal status, Fisher's exact test will be used.

17.4.1 Safety Analysis

The statistical analysis of this open label single arm trial of silicone gel-filled breast implants is consistent with the draft FDA "Points to Consider" document of August 1999. For all adverse events observed in this Core Gel Study the time to occurrence and time-weighted rate of freedom from complication will be analyzed by Kaplan-Meier survival analysis. Further, the time relationship of the complication will be modeled with Cox regression to examine risk factors for adverse events. The non-cumulative point prevalence and incidence per patient and per device will be calculated with associated exact 95% confidence intervals. If the same complication occurs in a patient on more than one follow-up visit and it is determined to be a new complication, that patient will be counted as having two adverse events of the same type.

17.4.2 Effectiveness Analysis

The breast size and chest/bust circumference will be compared at each follow-up examination to that at baseline. For the continuous measures, a paired t-test will be used for this analysis.

The psychometric variables will be analyzed consistent with the validation methods of the instrument. Since these measures are at least ordinal, repeated measures analysis of variance (paired t-test for only two time periods) will be used to compare the results of post-procedure follow-up examination results with that of baseline.

18.0 INVESTIGATOR SELECTION AND TRAINING

Each physician participating as an investigator in the clinical evaluation of the Mentor Round Low-Bleed Silicone Gel-filled Mammary Prosthesis must submit a copy of his/her medical license; a curriculum vitae for review by Mentor Clinical Programs; and sign an Investigator's Agreement (Attachment 7) stating his/her commitment to the terms of the agreement.

The CV should include the following information:

- Education (schools, dates, and degrees)
- Postgraduate training (institutions, dates, and nature of training)
- Teaching or research experience (institutions, dates and brief descriptions)
- Medical and professional experience (institutional affiliation, dates, and nature of practice)
- Pertinent publications (journals, titles, and identifying references)

Investigators selected for this clinical trial will be Board Certified in Plastic Surgery and have a current, unrestricted medical license. Investigators will be required to provide documentation of the number of gel breast implants and replacement implants they have performed. Investigators will be required to provide evidence that office operating rooms are accredited by the American Association of Accreditation of Ambulatory Surgical Facilities or other agency. Hospital operating rooms and outpatient surgery centers will be required to have accreditation as well.

Prior to enrolling patients in the study, each investigator must review the training materials provided by Mentor. Each investigator will be given an Investigator's Manual with copies of training materials arranged for reference and subsequent review. Also provided will be the telephone number(s) and address of the Medical Director, and the telephone number(s) and address to be used for reporting serious adverse events to Mentor.

19.0 INSTITUTIONAL REVIEW BOARD APPROVAL

Each site will have a designated principal investigator with co-investigators within the same practice. For each site, the principal investigator must secure Institutional Review Board (IRB) approval from each hospital or medical facility where the clinical study will be conducted.

This approval will cover all physicians designated as co-investigators within that practice. A copy of such written approval must be forwarded to Mentor before any prostheses can be shipped. As IRB approvals are received, the FDA will be notified in an IDE Supplement and the investigation at those centers can then be initiated.

An independent IRB may be used by those facilities that do not have their own IRB, but use of such an IRB is subject to prior approval of Mentor.

20.0 INFORMED CONSENT

Written informed consent must be obtained before each patient is entered into the study. Each investigator is to discuss in detail with the patient the surgical procedure associated with breast implantation.

The investigator should clearly explain that this is an elective procedure and should discuss the potential risks and benefits associated with silicone gel breast prostheses and alternative procedures. Patients should be advised that breast implants should not be considered lifetime implants due to the inherent nature of silicone implants, implant procedures, and potential physiological reactions.

The Patient Informed Consent must be signed before a patient can be enrolled in the study. A copy of this document appears in Attachment 3.

21.0 CONFIDENTIALITY

The identity of patients enrolled in the study and the information contained in their study records will be kept confidential by Mentor. As part of the investigator training session, investigators will be instructed in the importance of confidentiality and the techniques for protecting patients' privacy and rights.

Each patient will be assigned a study identification number to be used on study Case Report Forms (CRFs). The first three digits will correspond to the unique site number, and the last three will correspond to a patient number assigned by each investigator.

Confidentiality will be protected as much as possible throughout the study. Medical records will be reviewed by representatives of Mentor Clinical Programs and will be made available for review as required by the FDA and the IRB. Results of data collected will be reported as statistical information only. The patient's name will not be used or otherwise disclosed. If supporting documentation, such as a hospital procedure record, is requested, the site will copy it with patient identifying information concealed. Before sending these data to Mentor, the on-site clinical coordinator will enter the patient's study identification number on the top portion of each page.

Both investigators and patients will be made aware that, in unusual circumstances, the FDA or a court of law might request original patient records. In that instance, Mentor and/or the investigator would be required to comply.

22.0 INVESTIGATOR COMPLIANCE

In addition to the requirements of the protocol, investigators shall comply with all applicable state and federal laws, rules, and regulations. An investigator may be disqualified from participation in the study for failing to do so or for failing to comply with any of the requirements of this protocol. The procedure for disqualification will include suspension with time to correct deficiencies. Suspensions will be routinely reported to the investigator's IRB. In accordance with the Investigational Device Regulations, the FDA and the investigator's IRB will be notified if investigators are disqualified. No additional devices will be shipped to any investigator who has been disqualified or who is suspended at the time.

23.0 DATA SUBMISSION REQUIREMENTS

In order for the clinical investigation of this device to yield valid and significant data and to protect the well-being of the patients, careful and detailed record keeping is required by each investigator. To facilitate record-keeping, standard case report forms (CRFs) will be used. (See Attachment 10). They will be described in detail at the investigators training session as well as in written instructions to be distributed at that time. Each page of the CRFs will be NCR (no carbon required), allowing an original copy to remain at the site, while another original is sent to Mentor for data entry. A telephone number at Mentor will be available to investigators where they may call with questions about the study or the reporting forms as well as to report adverse events.

Inventory Control Log: The log will be located in the Investigator Notebook. During the study the investigator will record on the log the patient number for each unit used; if units are for any reason not used but removed from their packages, the investigator will also note that information, including the reason for wasted units. At the conclusion of the study, the Clinical Monitor will verify the number of used units against the inventory control log. The investigator will also retain the packing slips from each shipment.

Baseline: The Baseline CRF will include eligibility criteria, patient demographics, and physical examination results including vital signs and weight. A complete medical history will be obtained prior to the procedure, and the Rheumatic Disease Diagnosis Questionnaire will be completed. Breast measurements will be recorded and breast history will be record. Quality of Life Questionnaires will be administered.

Operative Record: This record will be filled out at the time the prosthesis is implanted and for any resurgery; it will include the date of the procedure, the size of the prosthesis, type of prosthesis, and the type of anesthesia used.

Secondary Procedures Record and Reimplantation Record: In the event of explantation, revision, or other reoperative procedure, the hospital operative report will be submitted with a Secondary Procedure record and a Serious Adverse Event Report. If a new prosthesis is implanted it will be recorded on the Reimplantation Record.

Follow-up Visits: At each scheduled post-operative visit, and at any unscheduled visits, the investigator will record the date and reason for the visit. If there are adverse events, they will be recorded on the Adverse Event Report. Any subsequent secondary procedures such as explantation, will be recorded on the Secondary Procedures Report and subsequent reimplantation will be recorded on the Reimplantation Report. The investigator will measure the breasts, assess nipple and breast sensitivity and capsular contracture. Quality of Life questionnaires and the Rheumatic Disease Diagnosis Questionnaire will be administered at the 1 Year, 2 Year, 4 Year, 6 Year, 8 Year and 10 Year visit.

End of Study Form: Whenever a patient leaves the study, whether voluntarily or involuntarily, reasons for discontinuation will be recorded. If possible, the evaluations that are done at the 24-month follow up visit would be done at the time of discontinuation.

Adverse Events Report: At the time of the implant procedure, as well as at each scheduled or nonscheduled visit, any adverse events reported by the patient or observed by the investigator will be recorded on the Adverse Event Report. The duration, severity, and attribution of each event will be recorded. The investigator will also note any resulting action or treatment.

Serious, unanticipated adverse events, are defined as any adverse occurrence, side effect, injury, toxicity, or sensitivity reaction that reasonably suggests adverse events from the implant which involve death, life threatening conditions or permanent impairment of body function which have not been addressed in the product literature or which has been addressed, but is occurring with unexpected severity or frequency. These include rheumatologic conditions. Serious, unanticipated adverse events will be reported to Mentor Clinical Monitor by telephone and the Adverse Event Report will be faxed to Mentor within 72 hours of receipt of report by physician, including, if applicable, information about death and/or hospitalization. Any operative procedure will be entered on the Adverse Event Report and all device ruptures will be entered on the Adverse Event Report.

24.0 REFERENCES

3. Hetter G. "Patient Satisfaction Following Augmentation Mammoplasty with the Gel Prosthesis", *Aesthetic Plastic Surgery* 3:251-259, 1979.
4. Strom S., Baldwin B., et al: Cosmetic Saline Breast Implants: A Survey of Satisfaction, Breast –Feeding Experience, Cancer Screening, and Health", *Plastic and Reconstructive Surgery*, 100: 1553-1557, November 1997.
5. Young VL, Nemecek J, Nemecek D, "The Efficacy of Breast Augmentation: Breast Size Increase, Patient Satisfaction, and Psychological Effects", *Plastic and Reconstructive Surgery* 94:958-969, 1994.
6. Gabriel SE, Woods J, et al: "Complications Leading to Surgery after Breast Implantation", *New England Journal of Medicine* 336:677-682, 1997.
7. Englert HJ, Brooks P., "Scleroderma and Augmentation Mammoplasty: A Causal Relationship?" *Australia New Zealand Journal of Medicine* 24:74-80, 1994.
8. Gabriel SE, O'Fallon, et al: "Risk of Connective-Tissue Diseases and other Diseases after Breast Implantation", *New England Journal of Medicine* 330:1697-1702, 1994.
9. Hochberg MC, Perlmutter DL, et al: "Lack of Association Between Augmentation Mammoplasty and Systemic Sclerosis (Scleroderma), *Arthritis Rheumatology* 39:1125-1131, 1996.
10. Burns CJ, Laing TJ, et al: "The Epidemiology of Scleroderma Among Women: Assessment of Risk from Exposure to Silicone and Silica", *Journal of Rheumatology* 23:1904-1911, 1996.
11. Goldman JA, Greenblatt R, et al: "Breast Implants, Rheumatoid Arthritis, and Connective Tissue Disease in a Clinical Practice", *Journal of Clinical Epidemiology* 48:571-582, 1995.
12. Strom BL, Reidenberg B, et al: "Breast Silicone Implants and Risk of Systemic Lupus-Erythematosus", *Journal of Clinical Epidemiology* 47:1211-1214, 1994.
13. Williams HJ, Weisman MH, Berry CC, "Breast Implants in Patients with Differentiated and Undifferentiated Connective Tissue Disease", *Arthritis & Rheumatology* 40:437-440, 1997.
14. Sanchez-Guerrero J, et al: "Silicone Breast Implants and the Risk of Connective Tissue Diseases and Symptoms", *New England Journal of Medicine* 332:1666-1670, 1995.

15. Shoaib BO, Patten BM, Calkins DS, ""Adjuvant Breast Disease: An Evaluation of 100 Symptomatic Women with Breast Implants or Silicone Fluid Injections", *Keio Journal of Medicine* 43: 79-87, 1994.
16. Shoaib BO, Patten MB, "Human Adjuvant Disease: Presentation as a Multiple Sclerosis-Like Syndrome" *Southern Medical Journal* 89:179-188, 1996.
17. Sanger JR, Kolachalam R, et al: "Short-term Effect of Silicone Gel on Peripheral Nerves: A Histologic Study", *Plastic and Reconstructive Surgery* 89:931-940, 1992.
18. Sanger. JR, Kolachalam R, et al: "Silicone Gel Infiltration of a Peripheral Nerve and Constrictive Neuropathy Following Rupture of a Breast Prosthesis", *Plastic and Reconstructive Surgery* 89:949-952, 1992.
19. Rosenberg NL, "The Neuromythology of Silicone Breast Implants", *Neurology* 46:308-314, 1996.
20. Ferguson JH, "Silicone Breast Implants and Neurologic Disorders Report of the Practice Committee of the American Academy of Neurology", *Neurology* 48:1504-1507, 1997.
21. Deapen DM, Brody GS, "The Relationship Between Breast Cancer and Augmentation Mammoplasty: An Epidemiologic Study", *Plastic and Reconstructive Surgery* 77:361-368, 1986.
22. Deapen DM, Brody GS, "Augmentation Mammoplasty and Breast Cancer: A Five Year Update of the Los Angeles Study", *Plastic and Reconstructive Surgery* 89:660-665, 1992.
23. Deapen DM, Brody GS, Augmentation Mammoplasty and Breast Cancer: A Five Year Update of the Los Angeles Study", *Journal of Clinical Epidemiology* 48:545-550, 1995.
24. Deapen DM, Brody GS, "Are Breast Implants Anticarcinogenic? A 14 Year Follow-up of the Los Angeles Study", *Plastic and Reconstructive Surgery* 89:660-665, 1997.
25. Berkel J, Birdsell DC, Jenkins H, "Breast Augmentation: A Risk Factor for Breast Cancer?", *New England Journal of Medicine* 326:1649-1653.
26. McLaughlin JK, Fraumeni JF et al: "Re: Breast Implants, Cancer, and Systemic Sclerosis (letter)", *Journal of the National Cancer Institute* 86:1424, 1994.
27. McLaughlin JK, Fraumeni JF et al, "Silicone Breast Implants and Risk of Cancer (letter)", *JAMA* 273:116, 1995.

28. UBTL, Inc. "A Reproduction/Teratology Study in Female Sprague-Dawley Rats Following Subcutaneous Implantation with Low Bleed Shell with Patch, Siltex Becker with Valve, RVT Smooth Shell with Diaphragm Valve and RTV Textured Shell with Mentor Leaf Valve", Final Report. UBTL No. 66325. Prepared for Mentor Corporation. May 23, 1994.
29. Siddiqui WH, et al: "Reproductive and Developmental Toxicity Studies of Silicone Gel Q7-2159A in Rats and Rabbits". *Fundamentals of Applied Toxicology* 23:370-376, 1994.
30. Siddiqui WH, et al, "Reproductive and Developmental Toxicity Studies of Silicone Elastomer Q7-2423/Q7-2551 in Rats and Rabbits", *Fundamentals of Applied Toxicology* 23:377-81, 1994.
31. Levine JJ, Howite NT, "Scleroderma-Like Esophageal Disease in Children Breast-Fed by Mother's with Silicone Breast Implants". *JAMA* 271:213-216, 1994.
32. Teuber SS, Gershwin ME, "Autoantibodies and Clinical Rheumatic Complaints in Two Children of Women with Silicone Gel Breast Implants", *Int. Arch. Allergy Immunol.* 103:105-108, 1994.
33. Lugowski S, Smith DC, et al: "Silicon Levels in Blood, Breast Milk, and Breast Capsules of Patients with Silicone Breast Implants and Controls". Fifth World Biomaterials Congress, May 29-June 2, 1996, Toronto, Canada.
34. Rasco DS, Greene WB, "The Absence of Esophageal Lesions In Maternal progeny of Silicone-Injected Rats", *Plastic and Reconstructive Surgery* 99:1784-1785, 1997.
35. European Committee on Quality Assurance and Medical Devices in Plastic Surgery (EQUAM). Consensus Declaration EQUAM – June 28, 1996.
36. Institute of Medicine (IOM) of the National Academy of Sciences Committee Report, "Safety of the Silicone Breast Implants, July 1999.
37. Brody G., "Safety of Breast Implants", *Plastic and Reconstructive Surgery*, vol 100, no.5, pp:1314-1321, October 1997.
38. Hennekens C, Lee M, et. Al: "Self-Reported breast Implants and Connective Tissue Diseases in Female Health Professionals", *JAMA* 275:616-621, 1996.
39. Schusterman M, Kroll S. et. al. "Incidence of Autoimmune Disease in Patients after Breast Reconstruction with Silicone Gel Implants versus

- Autogenous Tissue: A Preliminary Report”, *Ann. Plastic Surgery* 31:1-6, 1993.
40. Kern K, Flannery J, Kuehn P, “Carcinogenic Potential of Silicone Breast Implants” A Connecticut Statewide Study”, *Plast. Reconstructive Surgery* 100:737, 1997.
 41. Bryant H, Brasher P, “Breast Implants and Breast Cancer – Reanalysis of a Linkage Study”, *New Eng. J. Medicine* 332:1535, 1995.
 42. Brinton L, Malone K, Coates R, et. Al., “Breast Enlargement and Reduction: Results from a Breast Cancer Case-Control Study”, *Plast. Recon. Surgery* 97:269, 1996.
 43. Kjoller K, McLaughlin JK, Friis S, Blot William, Mellemkjaer L, Hogsted C, Winther J, Olsen, MD. “Health Outcomes in Offspring of Mothers With Breast Implants”, *Pediatrics* 102:5, November 1998, 1112-1115.
 44. Tairysh GV, Kuzbari R, Rigel S, Todoroff B, Schneider B, Deuting M, “Normal Cutaneous Sensibility of the Breast”, *Plastic and Reconstructive Surgery* 102:3, September 1998, 701-704.
 45. Slezak S, Dellon AL, “Quantitation of Sensibility in Gigantomastia and Alteration Following Reduction Mammoplasty”, *Plastic and Reconstructive Surgery* 91:7, June 1993, 1265-1269.
 46. Liew S, Hunt J, Pennington D, “Sensory Recovery Following Free TRAM Flap Breast Reconstruction”, *British Journal of Plastic Surgery* 49:4, 1996, 210-213.
 47. Vinnik CA. Migratory silicon - clinical aspects. Silicone in Medical Devices - Conference Proceedings. 1991 February 1-2; Baltimore, MD: U.S. Department of Health and Human Services, FDA Publication No. 92-4249 (p 59-67).
 - 47a. “Breast Implants: An Informational Update”, Food and Drug Administration, November 1998.
 - 47b. Robinson OG, Bradley EL, Wilson DS. Analysis of explanted silicone implants: A report of 300 patients *Ann Plast Surg* 1995; 34:1-7.
 48. Personal communication- S. Lori Brown, Ph.D., MPH, Research Scientist Officer, Office of Surveillance and Biometrics, CDRH, Epidemiology Branch, Rockville, Maryland 20850.

**ATTACHMENT 1
STUDY VISIT SCHEDULE**



**Table 1
STUDY VISIT SCHEDULE**

Data and Events to be Captured	Baseline	Operative Report ^A	Post-Operative Follow-up Visits and Forms ^H										
			6 Month (± 4 weeks)	1 Year Visit (± 6 weeks)	2 Year Visit (± 8 weeks)	3 Year Visit (± 16 weeks)	4 Year Visit (± 16 weeks)	5 Year Visit (± 16 weeks)	6 Year Visit (± 16 weeks)	7 Year Visit (± 16 weeks)	8 Year Visit (± 16 weeks)	9 Year Visit (± 16 weeks)	10 Year Visit (± 16 weeks)
Inclusion/Exclusion Criteria	X												
Patient Consent	X												
Demographics/Medical History/ Indication for Surgery/Breast History & Exam/Physical Exam	X												
Patient Registry		X											
Surgical Information		X											
Concomitant Medication	X		X	X	X	X	X	X	X	X	X	X	X
Breast Measurements	X		X	X	X	X	X	X	X	X	X	X	X
Mammography Results (if performed)	X		X	X	X	X	X	X	X	X	X	X	X
Postoperative Visit Report			X	X	X	X	X	X	X	X	X	X	X
Capsular Contracture Assessment			X	X	X	X	X	X	X	X	X	X	X
Nipple/Breast Sensitivity	X		X	X	X	X	X	X	X	X	X	X	X
Rheumatic Disease Questionnaire	X			X	X	X	X	X	X	X	X	X	X
Quality of Life Questionnaires ^C	X			X	X		X		X		X		X
Adverse Event ^G		X	X	X	X	X	X	X	X	X	X	X	X
Secondary Procedures and/or Reimplantation ^F			X	X	X	X	X	X	X	X	X	X	X
Magnetic Resonance Imaging ^{D,E}				X	X		X		X		X		X
End of Study ^B			X	X	X	X	X	X	X	X	X	X	X

^AWithin 30 days of screening
^BEnd of Study form is completed when patient completes all study visits, elects to drop, misses two consecutive visits, and/or is discontinued for other reasons
^CRosenberg Self Esteem Scale, SF-36, Tennessee Self-Concept Scale, Body Esteem Scale and Functional Living Index: Cancer (FLIC) for cancer patients
^DSubstudy of 405 randomly selected patients
^EAll patients with suspected silent rupture should be evaluated by MRI
^FDocument upon occurrence. Document all postoperative explanations, revisions, and other secondary procedures on Secondary Procedures Report. Report reimplantations on Re-Implantation Report
^GDocument upon occurrence by completing an Adverse Event Report
^HDocument any unscheduled post-operative visit on the Interim Visit form

ATTACHMENT 2
PRODUCT INSERT DATA SHEET



ROUND SILTEX[®] AND SMOOTH-SURFACE LOW-BLEED GEL-FILLED MAMMARY
PROSTHESES (CORE GEL STUDY)

102783-001 IDE REV

DEVICE DESCRIPTION

Two types of Mentor round Low Bleed Gel-filled Mammary Prosthesis will be used in the study: the Siltex textured surface device and the smooth surface device. Each implant is a silicone elastomer mammary device that is supplied individually packaged in a doubled wrapped packaging system, sterile, and non-pyrogenic. Each device consists of a silicone shell encasing a silicone gel filler material with a patch on the posterior side of the device. The basic smooth device shell consists of a crosslinked phenyl silicone elastomer layer sandwiched in between crosslinked methyl silicone elastomer layers. The phenyl layer acts as a barrier to slow the diffusion of any gel filler materials through the shell. The Siltex textured shell consists of a smooth shell to which is bonded an additional layer of silicone with a textured pattern imprinted into its surface. The Siltex shell is intended to provide a disruptive surface for connective tissue ingrowth. The gel filler is a crosslinked silicone polymer. All study devices will be manufactured from SiTech/NuSil silicone materials. Sizes for both Siltex (catalog # 354-XXXX) and Smooth-Surface (catalog # 350-7XXXBC) range from 100 to 800cc.

INCLUSION CRITERIA

1. Subject is genetic female, 18 years of age or older.
2. Candidate for:
 - Primary breast augmentation
 - Primary breast reconstruction (for cancer, trauma, surgical loss of breast or congenital deformity)
 - Revision surgery - (previous augmentation or reconstruction with silicone-filled or saline-filled implants).
3. Signs the Informed Consent.
4. Agrees to follow the procedures for explant analysis.
5. Agrees to comply with follow-up procedures, including returning for all follow-up visits.

EXCLUSION CRITERIA

Study subjects will not be allowed to enter the study if they have any of the following exclusion criteria:

1. Subject is pregnant.
2. Has nursed a child within three months of study enrollment.
3. Been implanted with any silicone implant other than breast implants (e.g. silicone artificial joints or facial implants).
4. Confirmed diagnosis of the following rheumatic diseases or syndromes: scleroderma, systemic lupus erythematosus, discoid lupus, rheumatoid arthritis, vasculitis, polymyositis, psoriatic arthritis, Reiter's syndrome, Lyme disease, ankylosing spondylitis, osteoarthritis, Raynaud's phenomenon, chronic fatigue syndrome, fibromyalgia, and Sjogren's syndrome.

5. Currently has a condition that could compromise or complicate wound healing (except reconstruction patients).
6. Subject in Augmentation cohort and has diagnosis of active cancer of any type.
7. Infection or abscess anywhere in the body.
8. Demonstrates tissue characteristics which are clinically incompatible with implant (e.g. tissue damage resulting from radiation, inadequate tissue, or compromised vascularity).
9. Possesses any condition, or is under treatment for any condition which, in the opinion of the investigator and/or consulting physicians(s), may constitute an unwarranted surgical risk.
10. Anatomic or physiologic abnormality which could lead to significant postoperative complications.
11. Demonstrates characteristics, which are unrealistic/unreasonable with the risks involved with the surgical procedure.
12. Premalignant breast disease without a subcutaneous mastectomy.
13. Untreated or inappropriately treated breast malignancy, without mastectomy.
14. Implanted metal or metal devices, history of claustrophobia or other condition that would make a MRI scan prohibitive.

WARNINGS

It is the responsibility of the surgeon, and Mentor relies on the surgeon, to advise the subject of all potential risks and complications associated with the proposed surgical procedure and device, including providing a comparison of the risks and complications of alternative procedures. Subjects should be advised that breast implants should not be considered lifetime implants. The life expectancy of the implant is unknown.

- Care should be taken not to damage the prosthesis with surgical instruments. Such contact may result in immediate or delayed rupture.
- This product is for single use only. The possibility of damage to the implant and infection exists if a subsequent procedure is performed (such as an open capsulotomy, breast pocket revision, etc.). It is the responsibility of the attending physician to determine if a new implant should be inserted. If the implant is damaged, it must be removed.
- Pre-existing infection should be treated and resolved before implantation of the prosthesis.
- Silicone gel can leak or "bleed" through the semipermeable silicone envelope into the capsule and adjacent breast tissue. Migration into capillaries has also been reported. The long-term effects of such "bleed" are unknown. Prospective subjects should be made aware of this potentiality.
- Only one prosthesis should be implanted per breast. Mentor recommends against the stacking of implants, one upon the other. The devices have not yet been tested for this use and the integrity of the implant cannot be guaranteed as the materials may abrade and wear. Such abnormal stress may result in weakening or rupture of the prosthesis.
- Do not insert or attempt to repair a damaged or altered prosthesis.
- The action of drugs (examples: antibiotics and steroids) in contact with the prosthesis has not been tested by the manufacturer and their use cannot be recommended. Each physician who chooses to use chemotherapeutic drugs with this prosthesis must assure compatibility of the drug with the silicone elastomer.
- In vitro testing has demonstrated that even low concentrations of Betadine solution placed in contact with the breast implant will compromise implant integrity in the long term. Therefore, we recommend that no Betadine solution or other antibacterial, antiseptic, or cleaning agent be used in contact with the device.

If a cleaning solution is to be used within the implant surgical space, the site should be carefully rinsed to remove the residual solution.

- Preoperative evaluation of the implant design and implant site should include allowances for adequate tissue coverage. Pressure, force, tension and other stresses to which the implant site will be susceptible must be considered.
- Sepsis, hemorrhage or thrombosis may result from the placement of any foreign object in the body.
- The use of microwave diathermy in subjects with breast implants has been reported to cause tissue necrosis, skin erosion and extrusion of the implant. Its use in subjects with breast implants is not recommended.
- **The subject should be made aware that any abnormal stress or trauma to the breast could result in rupture of the prosthesis.**
- Mentor recommends against the treatment of capsule firmness by forceful external stress (such as closed capsulotomy) and is not responsible for the structural integrity of the implant should the surgeon elect to perform such a procedure.
- The American College of Radiology has stated that mammography may be less effective on implanted breasts. The mammographer should be trained and experienced with the most current radiologic techniques and equipment. This may increase cost and radiation exposure to the subject. Subjects should be instructed how to distinguish the prosthesis from normal or abnormal breast tissue during self-examinations for breast cancer.
- Careful hemostasis is important to prevent postoperative hematoma formation. Should excessive bleeding persist, it is recommended that the device not be implanted until the bleeding is controlled.
- If a physician treats a hematoma or serous fluid accumulation by aspiration, or if a biopsy or lumpectomy is performed, care must be taken to avoid damaging the implant. These procedures present possible risk of implant puncture.
- The incidence of extrusion of the prosthesis has been shown to increase when the prosthesis has been placed in injured areas: scarred, heavily irradiated or burned tissue, crushed bone areas or where severe surgical reduction of the area has previously been performed.
- Excessive fibrous capsular formation or contracture may occur around any implant placed in contact with soft tissues. The incidence and severity of this occurrence may increase if postoperative local hematoma or infection occurs.
- The physician should use personal discretion when deciding to use these prostheses regarding subjects who exhibit psychological instability.
- It is possible for a granuloma to form around a tiny amount of silicone. Although these lumps are non-cancerous, they can be difficult to distinguish from cancerous lumps without being removed (biopsied) and examined.
- The FDA believes there is currently inadequate research on the relationship, if one exists, between birth defects and silicone implants.
- **Surgical implantation of a mammary prosthesis may interfere with the ability to breast feed. However, it should be noted that previous breast reconstruction surgery, such as mastectomy, may be the initial cause of this interference.**

PRECAUTIONS

- It is the responsibility of the surgeon to advise prospective subjects or their representatives, prior to surgery, of the possible complications associated with the use of this product.
- Mentor recommends the surgeon consider implant size and the firmer nature and higher profile of the Siltex shell when choosing optimum incision size and surgical approach.

Certain surgical approaches may cause higher stresses on the device during implantation.

- Avoid too small an incision. A larger incision than is normally used for other smooth-surface, saline-filled mammary implants may be required to facilitate insertion and to avoid damage to the device. A device which is damaged during insertion may result in postoperative rupture.
- Any surgeon performing augmentation or reconstructive mammoplasty with implants should be familiar with the currently available techniques for measuring the subject, determining the implant size and performing surgery.
- Lint, dust, talc, surgical glove powder, drape and sponge lint, fingerprints, skin oils and other surface contaminants deposited on an implant by improper handling may cause foreign body reactions. Strict adherence to clean, aseptic techniques should be maintained to prevent contamination of the implant and possible complications. Surgical instruments and gloves should be rinsed clean of any impurities before handling the implant.
- The silicone elastomer shell may be easily cut by a scalpel or ruptured by excessive stress, manipulation with blunt instruments or penetration by a needle. Subsequent rupture may result. All products should be carefully inspected for structural integrity prior to and during implantation.
- Meticulous care must be exercised in handling and implanting the device.
- Any subsequent surgical procedures in the area of the implant should be undertaken with extreme caution as damage to the implant could occur. In the event that an implant is damaged, it must be removed.
- Each device should be checked for patency prior to surgery and continuously monitored throughout the surgical procedure to ensure the structural integrity of the device is not compromised in any way. This prosthesis should not be implanted following any modifications to its original design. A prosthesis which has been damaged, or on which repairs or modifications have been attempted, should not be implanted. A standby prosthesis should be available at the time of surgery.
- Do not use disposable, capacitor-type cautery devices as damage to the outer shell of the prosthesis may result.

ADVERSE EVENTS

Any subject undergoing a surgical procedure is subject to possible unforeseen operative and postoperative complications. Potential reactions and complications associated with the use of Siltex or smooth-surface gel-filled mammary prostheses should be discussed with and understood by the subject prior to surgery. It is the responsibility of the surgeon, and Mentor relies on the surgeon, to provide the subject with this information and to weigh the risk/benefit potential for each subject.

SURGICAL RISKS OF THE PROCEDURE

All surgical procedures have a small risk of complication inherent to the surgery itself and to anesthesia. These risks include:

Infection

Severe infection on rare occasions results in Toxic Shock Syndrome or TSS. An infection can result from any surgery and produce swelling, tenderness, pain and fever. Almost all infections appear within a few days of the operation but may appear at any time after surgery.

Hematoma

Formation (a collection of blood in the surgical area)

Seroma

Fluid accumulation around the implant which may or may not require removal). The body will absorb both areas of fluid accumulation (seromas) and small hematomas, but large ones may have to be drained surgically to permit proper healing.

Scarring

Any incision in the skin will leave a scar that is permanent. While surgeons will use plastic surgical techniques to make this as inconspicuous as possible, some patients have a skin quality that results in more conspicuous scars no matter how the incision is repaired.

Anesthetics

There are risks from anesthetics as well.

RISKS SPECIFIC TO BREAST IMPLANTS

Risks specific to breast implants include:

Capsular Contracture

Capsular contracture is the most common side effect of breast implants. To accept the implant, a surgical pocket behind the breast is made somewhat larger than the implant itself. Normally a healing scar forms an envelope around the implant, which, on occasion, will shrink sufficiently to squeeze the implant, producing varying degrees of firmness. The implant can feel hard, be painful and/or distorted. This can occur soon after surgery or years later and may be unilateral, bilateral or asymmetric. Surgical release or excision of the scar is often successful but recurrence is not uncommon. The cause of the contracture phenomenon is poorly understood and is probably related to an idiosyncratic response to the presence of normal, benign skin bacteria, *Staphylococcus epidermidis*. In the past, closed disruption of the scar by squeezing the breast was common, but this is rarely practiced today. This practice will be prohibited in this study. Capsular contracture is graded in severity on a scale of I to IV by Baker classification.

Calcification of the capsule can also occur. This is usually associated with Grade IV contracture. Calcification is a phenomenon that is occasionally seen with long term scarring especially if there is irritation such as tight burn scars that cross joints. Calcified capsules may require removal if the patient wishes relief from her contracture but otherwise seem to be harmless. Small foci of calcification are commonly seen anywhere in the breast parenchyma. They can usually be identified as benign by the radiologist but on occasion may require biopsy to rule out a malignancy. These do not seem to be more common in the augmented patient.

Deflation/Rupture/Leakage

Breast implants **are not lifetime devices** and cannot be expected to last forever. Some implants deflate or rupture in the first few months after being implanted and some deflate after several years; others are intact 10 or more years after the surgery.

a. Silicone Gel-Filled Breast Implants – When silicone gel-filled implants rupture, some women may notice decreased breast size, nodules (hard knots), uneven appearance of the breasts, pain or tenderness, tingling, swelling, numbness, burning, or changes in sensation.

Other women may unknowingly experience a rupture without any symptoms (i.e., “silent rupture”). Magnetic resonance imaging (MRI) with equipment specifically designed for imaging the breast may be used for evaluating patients with suspected rupture or leakage of their silicone gel-filled implant.

Silicone gel which escapes the fibrotic capsule surrounding the implant may migrate away from the breast. The free silicone may cause lumps called granulomas to form in the breast or other tissues where the silicone has migrated, such as the chest wall, armpit, arm, or abdomen.

Plastic surgeons usually recommend removal of the implant if it has ruptured, even if the silicone is still enclosed within the scar tissue capsule, because the silicone gel may eventually leak into surrounding tissues. If you are considering the removal of an implant and the implantation of another one, be sure to discuss the benefits and risks with your doctor.

FDA completed a retrospective study on rupture of silicone gel-filled breast implants.¹ This study was performed in Birmingham, Alabama and included women who had their first breast implant before 1988. Women with silicone gel-filled breast implants had a MRI examination of their breasts to determine the status of their current breast implants.

The 344 women who received a MRI examination had a total of 687 implants. Of the 687 implants in the study, at least two of the three study radiologists agreed that 378 implants were ruptured (55%). This means that 69% of the 344 women had at least one ruptured breast implant. Of the 344 women, 73 (21%) had extracapsular silicone gel in one or both breasts. Factors that were associated with rupture included increasing age of the implant, the implant manufacturer, and submuscular rather than subglandular location of the implant. A summary of the findings of this study is also available on FDA's website at <http://www.fda.gov/cdrh/breastimplants/studies/biinterview.pdf> and <http://www.fda.gov/cdrh/breastimplants/studies/birupture.pdf>.

Robinson et al. studied 300 women who had their implants for 1 to 25 years and had them removed for a variety of reasons.² Visible signs of rupture in 51% of the women studied were found. Severe silicone leakage (silicone outside the implant without visible tears or holes) was seen in another 20%. Robinson et al. also noted that the chance of rupture increases as the implant ages.

Other studies indicate that silicone may escape the capsule in 11-23% of rupture cases.^{3,4,5,6}

¹ Brown SL, Middleton MS, Berg WA, Soo MS, Pennello G. Prevalence of rupture of silicone gel breast implants in a population of women in Birmingham, Alabama. *American Journal of Roentgenology* 2000, 175-1-8.

² Robinson OG, Bradley EL, Wilson DS. Analysis of explanted silicone implants. a report of 300 patients. *Ann Plast Surg.* 1995, 34.1-7

³ Vinnik CA. Migratory silicone – clinical aspects. *Silicone in Medical Devices – Conference Proceedings* 1991 February 1-2; Baltimore, MD: U.S. Department of Health and Human Services, FDA Publication No 92-4249 (p 59-67).

For the Core Gel Study, a randomly selected subset of 405 patients will undergo MRI scans at 1, 2, 4, 6, 8, and 10 years. The purpose of this substudy is to determine the rate of silent rupture. Scans will be sent to a central reading center to be read by an independent breast MRI radiologist. This radiologist will be blinded to the patient name and site. The results will be entered into the study database. All patients, whether or not they are randomized to undergo MRI scans, will be directed to see their physician whenever the patient believes a rupture has occurred.

Gel Bleed

The gel in an implant consists of a three-dimensional crosslinked structure that constitutes about 15 % of the total volume. The interstices are filled with silicone oil. This oil is similar to the materials available in many products including anti-gas medication, available without prescription for infants and adults. The shell of the implant is slightly permeable to the oils. Depending on the age, brand, chemical characteristics and environmental mechanics of a given device, varying small amounts of the oil diffuses or “bleeds” through the shell. Some amount diffuses into the scar envelope where it can be picked up by macrophages, the probable mechanism by which it is transported into regional lymph nodes.

The oil has been detected in the breast and surrounding subcutaneous tissues in amounts diminishing with distance. It is assumed that minute amounts of silicone from all ingested and injected sources are distributed throughout the body. Because silicone is hydrophobic, it is unlikely to be transported by any mechanism other than macrophage migration or local diffusion. There is no evidence to suggest that the gel contents have any different metabolic effect on the body than the solid silicone envelope.

Changes in Nipple and Breast Sensation/Breast Pain

Any surgery of the breast can result in undersensitive or oversensitive nipple-areolar complexes and/or undermined areas of breast skin. These changes can vary in degree and may be temporary or permanent. Changes in nipple/breast sensation may, on occasion, affect sexual response or comfort while nursing. These changes are believed to be a result of nerve damage from the surgery and not the presence of the implant itself.

Most women undergoing augmentation or reconstruction with a mammary prosthesis will experience some breast and/or chest pain postoperatively. While this pain normally subsides in most women as they heal after surgery; it can become a chronic problem in other women. Chronic pain can be associated with hematoma, migration, infection, and implants that are too large or capsular contracture. Sudden severe pain may be associated with implant rupture.

Interference with Mammography in Detection of Cancer

As silicone is opaque to x-rays, an implant may interfere with the early detection of cancer by mammography as it may obscure part of the breast.

⁴ Duffy MJ, Woods JE. Health risks of failed silicone gel breast implants: a 30-year clinical experience. *Plast Reconstr Surg* 1994;94:295-299

⁵ Berg WA, Caskey CI, Hamper UM, Kuhlman JE, Anderson ND, Chang BW, Sheth S, Zerhouni EA. Single- and double-lumen silicone breast implant integrity: Prospective evaluation of MR and US criteria. *Radiology* 1995;197:45-52

⁶ Gorczyca DP, Schneider E, DeBruhl ND, Foo TKF, Ahn CY, Sayre JW, Shaw WW, Bassett LW. Silicone breast implant rupture: Comparison between three-point Dixon and fast spin-echo MR imaging. *AJR* 1994;162:305-310

Newer techniques of breast compression improve the amount of breast that can be visualized. Alternatively, most surgeons feel that the device may improve the detection of tumors by palpation. While of considerable theoretical concern, delayed detection due strictly to the presence of an implant has not been reported. Women at high risk of developing breast cancer should consider getting implants with caution. Since the breast is compressed during mammography, it is possible for the implant to rupture, but this is rare and should not deter a woman from regular, routine mammographic screening. Before the mammography exam, women should inform the technologist that they have implants.

Calcium Deposits

Calcium deposits are seen occasionally in old scars anywhere in the body and this is true of the implant capsule. This usually does not occur until years after implant surgery. Benign calcifications are also commonly seen on mammography in otherwise normal breast parenchyma even in breasts that have never been operated on. These benign calcium deposits usually have a different x-ray appearance than the calcifications that signal a malignancy.

An expert radiologist can usually determine if a calcium spot is benign or malignant but occasionally a biopsy may be necessary to rule out malignancy. There is no evidence that these deposits occur more or less frequently in women with implants than those who have not received implants.

After many years, some patients may develop a thin layer of calcium in the scar capsule that surrounds the implant. This is almost always associated with capsular contracture but otherwise causes no known problem. (Please see capsular contracture section for information on risk of developing calcium deposits with implants)

Delayed Wound Healing

In some cases, the incision site fails to heal normally.

Extrusion

Unstable or compromised tissue covering and/or interruption of wound healing may result in extrusion, which is when the breast implant comes through the skin.

Necrosis

Necrosis is the formation of dead tissue around the implant. This may prevent wound healing and require surgical correction and/or implant removal. Permanent scar deformity may occur following necrosis. Factors associated with increased necrosis include infection, use of steroids in the surgical pocket, smoking, chemotherapy/radiation, and excessive heat or cold therapy.

Breast Tissue Atrophy/Chest Wall Deformity

The pressure of the breast implant may cause the breast tissue to thin and shrink. This can occur while implants are still in place or following implant removal without replacement.

Dissatisfaction with Cosmetic Results

Visible and/or palpable wrinkles in an implant are related to the thinness of the overlying tissue cover, the degree of capsular contracture and the texturing of the implant shell surface. Traditional smooth walled gel devices rarely demonstrate wrinkles.

Surgical error, preexisting asymmetry or deformity, keloid formation of the incisional scar, vagaries of time, weight gain or loss, pregnancy and nursing can all contribute to an immediate or late poor aesthetic result. With time most breasts, with or without implants, become ptotic to some degree. Asymmetry is usually related to the inability to totally correct for pre-existing disparity between the two breasts. It can also be attributed to surgical error, asymmetric contracture, or rupture of the implant.

Excessive buildup of collagen at the incision site during the healing process causes some patients to develop scars of cosmetic concern. Keloid scars, which do not respond well to treatment, often extend beyond the edges of the original scars and can continue to enlarge over time. Hypertrophic scars are generally confined to the original site and respond well to scar revision treatment, which may include steroid injections to break down the collagen or surgery to revise the position, direction or line of the scar.

Granulomas

It is possible for a granuloma to form around a tiny amount of silicone. Although these lumps are non-cancerous, they can be difficult to distinguish from cancerous lumps without being removed (biopsied) and examined.

Resurgery: Women should understand there is a high chance they will need to have additional surgery at some point to replace or remove the implant. Also, problems such as rupture, capsular contracture, infection, shifting, and calcium deposits can require removal of the implants. Many women decide to have the implants replaced, but some women do not. Those who do not may have cosmetically unacceptable dimpling and/or puckering of the breast following removal of the implant.

UNKNOWN RISKS

The issue of the possible relationship between silicone (and other implantable materials) and various diseases has been the subject of significant scientific debate. Concerns include immunological and neurological disorders, carcinogenicity and connective tissue disorders.

Connective Tissue Disease

The term Connective Tissue Disorder has been used to describe a variety of symptoms thought to be related to silicone breast implants. Some cases of these disorders have been reported in women with breast implants, and some of these women have reported a reduction in symptoms after their implants have been removed. Several studies have explored whether a possible link exists between silicone breast implants and connective tissue disorders or other immunological diseases.

Neurological Disorders

Co-incident neurological problems such as multiple sclerosis and amyotrophic lateral sclerosis (ALS) have occurred in a small number of breast implant patients.

Cancer

Case reports in the medical literature have associated tumors with the presence of silicone breast implants. Several studies have been conducted to determine the carcinogenic risk of breast implants and no evidence of increased risk of cancer has been demonstrated. Continuing assessment of both known and possible carcinogenic risks associated with breast implant surgery is ongoing.

Birth Defects

No credible reports on birth defects or other reproductive effects in humans associated with implantation of silicone mammary prostheses of any type have been identified in the literature. Recent studies provide further evidence that silicone materials used in mammary prosthesis do not cause adverse reproductive effects in experimental animals.

Breast Feeding

Although any breast surgery, including breast implantation, could theoretically interfere with the adequacy of the woman's milk supply, many women with breast implants have nursed their babies successfully. It is known that any breast surgery such as breast biopsy can affect the quantity of milk produced.

In recent years, the question has been raised regarding the potential transfer of silicone into the breast milk of women with silicone breast prostheses and possible effects on the health of breast fed children.

However, more recent studies have provided strong evidence of the lack of association between silicone breast implants and adverse effects in breast fed children.

SUBJECT REGISTRY

All Core Gel Study subjects will become part of the Core Gel Study Registry. The information in the registry will allow the subjects to be contacted directly or through their implanting surgeon. The information contained in the registry will include subject name, Social Security Number, mailing address, and phone number.

PRODUCT EVALUATION

Mentor requests that any adverse and/or explantation resulting from the use of this device be brought to the immediate attention of the Clinical Programs Department of Mentor, 201 Mentor Drive, Santa Barbara, CA 93111USA. Clinical Programs will contact the Product Evaluation Department at Mentor, in Irving, TX.

If explantation is necessary, Mentor will analyze the explanted and retrieved device, and the subject and physician will be asked to allow Mentor to perform tests that might alter the condition of the device. The Core Gel Retrieval Protocol will be utilized to evaluate explanted devices from enrolled in this study.

RETURNED GOODS AUTHORIZATION

Authorization must be received from Mentor prior to the return of merchandise. Merchandise returned must have all manufacturer's seals intact and be returned within 30 days from date of invoice to be eligible for credit or replacement. Please contact the Mentor Aesthetic Products Customer Service Department for details.

To obtain a Return Authorization Number call (800) 235-5731, or FAX (805) 967-7108. Returned products may be subject to restocking charges. Mentor does not accept returns on Special Order Devices.

PRODUCT INFORMATION DISCLOSURE

Mentor expressly disclaims all warranties, whether written or oral, statutory, express or implied, by operation of law or otherwise, including, but not limited to, any implied warranties of merchantability, fitness or design.

Mentor shall not be liable for any direct, incidental or consequential loss, damage or expense, directly or indirectly arising from the use of this product. No representation or other affirmation of fact, including but not limited to statements regarding suitability for use, or performance of the product shall be or be deemed to be a warranty by Mentor for any purpose. Mentor neither assumes nor authorizes any other or additional liability or responsibility in connection with this product.

PRODUCT ORDER INFORMATION

U.S. Customers

To order, please contact the Mentor Aesthetic Products Customer Service Department at Mentor, 201 Mentor Drive, Santa Barbara, CA 93111. Toll free telephone (800) 235-5731. FAX (805) 967-7108.

CAUTION: Investigation device. Limited by Federal law to investigational use.

This product is to be used only by a physician participating in an Investigational Device Exemption (IDE) Core Study Sponsored by Mentor.

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

REFERENCES

Literature references are available upon request from:

Mentor
Marketing Services, Literature Department
201 Mentor Drive
Santa Barbara, CA 93111 USA



MENTOR

For customer service or to return product, please call
(800) 235-5731 in USA; outside USA call (805) 879-
6000

Manufacturer
Mentor
Irving, TX 75038 USA

**ATTACHMENT 3
INFORMED CONSENT**

Informed Consent

Participation as a Research Subject in the "Study of the Safety and Effectiveness of the Mentor Round Low-Bleed Silicone Gel-filled Mammary Prosthesis in Women Undergoing Primary Breast Augmentation, Reconstruction or Revision (Core Gel Study)"

Sponsor: Mentor, 201 Mentor Drive, Santa Barbara, CA 93111 USA

Patient: _____ Study ID: _____

Principal Investigator: _____

1. PURPOSE AND BACKGROUND OF THIS STUDY

You are being asked to take part in a research study of breast implants. This study is sponsored by Mentor, a manufacturer of plastic surgery products. The purpose of this study is to determine the safety and effectiveness of the smooth and textured surface Mentor Round Low-Bleed Silicone Gel-filled Mammary Prosthesis in women who are undergoing primary breast augmentation, primary breast reconstruction or revision. For example, safety information on the rate of capsular contracture, rupture, and infection will be collected, and used to help determine device safety. These implants are investigational devices. This Consent form gives you information about your breast implant procedure and your participation in this study. Your signature verifies that you have read this document and received a copy.

Approximately 1000 patients at centers across the United States will be enrolled in this research study. These patients will be implanted with silicone breast prostheses and monitored for 10 years to collect information on risks associated with the implant surgery as well as changes in the way these patients feel about themselves.

Breast implants have been used in nearly two million women since the early 1960s. There are known risks and potential complications from having breast implants. Since 1992 the Food and Drug Administration (FDA) has allowed limited silicone gel implants to clinical studies of breast reconstruction after mastectomy for cancer, correction of deformities, or replacement of damaged implants. The FDA has not formally approved these gel-filled breast implants as safe and effective because additional scientific evidence needs to be collected. Your participation will help answer the remaining questions.

Your participation is voluntary.

2. ELIGIBILITY REQUIREMENTS

INCLUSION CRITERIA

You will be allowed to enter the study if the following criteria are met:

- You were born female and 18 years of age or older.

- Are a candidate for one of the following:
 - Primary breast augmentation (general breast enlargement or sagging after breast feeding)
 - Primary breast reconstruction (for cancer, trauma, surgical loss of breast or congenital deformity)
 - Revision surgery (if you currently have a silicone filled implant or a saline filled implant).
- Sign the Informed Consent
- Agree to follow the procedures for explant analysis.
- Agree to comply with the follow-up procedures, including returning for all follow-up visits.

EXCLUSION CRITERIA

You will *not* be allowed to enter the study if you meet any of the following criteria:

- You are pregnant.
- Have nursed a child within three months of this study enrollment.
- Have been implanted with any silicone implant other than breast implants (e.g. silicone artificial joints or facial implants).
- Have a confirmed diagnosis of the following rheumatic diseases or syndromes: SLE, Sjogren's syndrome, scleroderma, polymyositis, or any connective tissue disorder, rheumatoid arthritis, crystalline arthritis, infectious arthritis, spondyarthropathies, any other inflammatory arthritis, osteoarthritis, fibromyalgia, or chronic fatigue syndrome.
- Currently have a condition that could increase risk or complicate wound healing (except reconstruction patients).
- Are an Augmentation patient and have a diagnosis of active cancer of any type.
- Have an infection or an accumulation of pus in a body tissue (abscess), anywhere in the body.
- Have a tissue condition that is clinically incompatible with the implant (e.g. tissue damage resulting from radiation, inadequate tissue, or compromised vascularity).
- Have any condition, or are under treatment for any condition, that your doctor determines to be an unwarranted surgical risk.
- Have a physical abnormality that could lead to significant postoperative complications.
- Have characteristics that are unrealistic/unreasonable with the risks involved with the surgical procedure.
- Have a premalignant breast disease without a subcutaneous mastectomy.
- Have untreated or inappropriately treated breast cancer, without mastectomy.
- Have an implanted metal or metal devices, history of claustrophobia, or other condition that would make a MRI scan prohibitive.

You should ask your doctor to clarify any terms you do not understand. Also, your doctor must provide a copy of this document to you.

3. DEVICE DESCRIPTION

Two types of Mentor Round Low-Bleed Silicone Gel-filled Mammary Prostheses will be used in the study: the Siltex textured surface device and the smooth surface device. Each implant is a silicone elastomer (rubber) mammary device that is supplied individually packaged in a doubled wrapped packaging system, sterile, and non-pyrogenic (does not cause fever). Each device consists of a silicone shell encasing a silicone gel filler material with a patch on the posterior side of the device. The basic smooth device shell consists of a silicone layer sandwiched in between two other silicone layers. This construction acts as a barrier to slow the diffusion of (spread) any gel filler materials through the shell. The Siltex textured shell consists of a smooth shell to which is bonded an additional layer of silicone with a textured pattern imprinted into its surface. The Siltex shell is intended to prevent tissue ingrowth. The implants will be available in sizes 100cc through 800ccs.

Your plastic surgeon will discuss these implants with you and explain why a particular implant may be best suited for you.

4. SECOND OPINIONS

If any problems or complications occur during the study, you may be asked or wish to obtain second opinions. You have the right to consult a physician of your choice.

5. STUDY PROCEDURES

You will talk about your procedure and participation in this Study with your doctor, in advance, and you should take sufficient time to think about your participation. You should check with your insurance company prior to the operation, as the surgery may affect your coverage.

Your participation in this study will be for a period of ten years. You will be seen at 6 months, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 years. It is very important that you come back for **all** postoperative visits, as the information obtained from those exams is extremely important in the study of these devices.

For patients who have undergone breast implantation either as a cosmetic or a reconstructive procedure, health insurance premiums may increase, coverage may be dropped, and/or future coverage may be denied. Treatment of complications may not be covered as well. Check with your insurance company regarding these coverage issues.

Baseline

If you agree to be in this research study, you will first have to be examined by your doctor to determine if you are a good candidate and if you are eligible. This screening may involve referral to other specialists. Follow-up visits to other specialists may also be required. During this visit, a medical history and physical examination will be completed.

Your doctor will ask you questions about any rheumatology diseases and symptoms you might have and you will be asked to fill out quality of life questionnaires.

Rheumatology Assessment

Your doctor will administer a rheumatic disease diagnosis questionnaire prior to your surgery. This is required to provide information about the possible relationship breast implants may have with connective tissue disorders, arthritis and rheumatic conditions. This questionnaire will be administered again at the 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10 year visits after your surgery.

Quality of Life Questionnaires

You will be asked to complete Quality of Life questionnaires prior to your surgery. These are “paper and pencil” questionnaires, which will take approximately 30 minutes to complete. These are required to measure how you feel about your body before and after your breast implant procedure and are a very important part of the research. You will be asked to complete these questionnaires again at the 1, 2, 4, 6, 8, and 10 year visits after your surgery.

Description of the Operation

A surgeon using accepted standards of practice will perform your operation. The operation may be performed in a physician’s office, a hospital operating room or in an outpatient surgical center. Hospitalization may or may not be required. Your doctor will explain the particular type of implant that will be used, how and where it will be placed and the type of anesthesia to be used. He/she will also give you an overall description of the operation.

You may require surgery to correct any complications that may arise or revisions such as change in implant size that you may request.

Follow-up Visits

After your surgery, you will be asked to make visits at the following time periods after the surgery: 6 months, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10 years. Each visit will take about 60 minutes. Your doctor will perform an evaluation of the status of the implant and you will be examined for the presence of any post –surgical complications.

You are making a commitment to continue in the study for the duration and to complete all of these follow-up visits. The information obtained from these visits is important in the study of these breast implants. If you move, arrangements will be made with your doctor for follow-up with another doctor in your area.

Magnetic Resonance Imaging (MRI)

Breast implants may not last a lifetime. The shell may rupture due to wear and tear, or direct injury. Rupture should be suspected if there is a change in character of the implant such as a new, persistent burning sensation on one side or a change in softness, texture or shape of the implant and may be difficult to diagnose without surgical exploration or a magnetic resonance imaging (MRI) scan. This type of examination produces a picture of your breasts without using x-rays and is commonly used in the x-ray departments of most hospitals to detect problems in bones, lungs and all other areas of the body.

The MRI scan has been determined to be the best way to find out if your implant has ruptured without performing surgery. In order to detect a "silent rupture" (a rupture without any symptoms or visible changes), you may be in a subset of patients who will undergo an MRI scan at 1, 2, 4, 6, 8, and 10 years after your surgery. If you do, you will have to lay on your stomach with your breast in a special holder. You will then be placed in the machine, which may be open or may be like going into a tunnel. Some patients experience an uneasiness at being in a closed space. While the machine is taking images of your breast, it will make a noise. In order to have an MRI scan, you must not have any implanted metal or metal devices in your body, or a history of claustrophobia. The procedure should take about an hour. Mentor will pay for the MRI scans.

Any patient who is suspected of having a ruptured implant while in the study will be examined by her doctor and undergo an MRI scan to see if her implants are ruptured. Mentor will pay for these MRI scans.

6. IMPLANT REGISTRY

As a participant in this study you will be asked to participate in the breast implant patient registry. This will allow Mentor to notify you, if necessary, of any new information about the safety of your silicone-filled breast implant(s). Every effort will be made to keep the information in the registry confidential and that information will only be provided to the FDA upon their request. However, under certain circumstances, Congress has the right to get clinical data from the FDA or a court could order disclosure of certain information that could include your clinical study records.

Your doctor will provide you with identification information, which pertains to your implant(s) after your surgery. This will let you know what type of implant you have. This should be kept with your important papers for future reference. You should also remain in contact with your doctor to get current important information or, if you leave your doctor, you should leave a forwarding address.

7. BENEFITS OF BREAST IMPLANTS

Breast augmentation surgery is elective surgery designed to improve your appearance. Women with breast cancer have reported that breast reconstruction with mammary implants has aided in their recovery from breast cancer and has reduced emotional stress by helping to return their body to a more natural appearance.

You may benefit other women by providing information about possible health problems associated with breast implants and to help demonstrate the safety and effectiveness of the device. There are no direct additional benefits to you beyond receiving this implant.

8. RISKS AND DISCOMFORTS OF THE OPERATION

Breast surgery requires an incision. As with any surgical procedure, there are risks such as:

Infection: (severe infection on rare occasions results in Toxic Shock Syndrome or TSS). An infection can result from any surgery and produce swelling, tenderness, pain and fever. Almost all infections appear within a few days of the operation but may appear at any time after your surgery. If you get a serious infection, which doesn't go away with antibiotics, your implant may have to be removed.

Hematoma Formation: a collection of blood in the surgical area.

Seroma: (fluid accumulation around the implant which may or may not require removal). Your body will absorb both areas of fluid accumulation (seromas) and small hematomas, but large ones may have to be drained surgically to permit proper healing. Surgical techniques, under most circumstances, can minimize though not eliminate them.

Scarring: Any incision in the skin will leave a scar that is permanent. While your surgeon will use plastic surgical techniques to make this as inconspicuous as possible, some patients have a skin quality that results in more conspicuous scars no matter how the incision is repaired.

There are risks from anesthetics as well.

9. RISKS AND DISCOMFORTS OF BREAST IMPLANTS

Breast implants have certain specific risks and complications, which may include:

Capsular Contracture: The normal healing scar membrane that forms around the implant can, in some women, tighten and squeeze the implant. This can cause the implant to feel firm. This firmness can range from slight to quite hard and the firmest ones can cause varying degrees of discomfort or pain. In addition to the firmness capsular contracture can result in a misshapen breast, visible surface wrinkling and/or displacement of the implant. Detection of breast cancer by mammography may also be more difficult.

If you wish to have this contracture softened, the scar tissue can be released or removed by making an incision into the breast during an operation called an Open Capsulotomy.

Your surgeon may recommend a technique called a closed capsulotomy in which he/she will apply forceful external pressure to the breasts to "break up" the scar tissue. Mentor does not recommend this technique because it could result in several complications such as breakage of the implant, bleeding, displacement of the implant resulting in asymmetry or distortion.

Your surgeon will explain the possible complications, as well as help you determine the best method for correcting capsular contracture.

Calcification of the capsule surrounding the implant can also occur. This can contribute to the hardening of the tissue and may be painful. Sometimes it may be necessary to remove the implant and/or the calcified capsule.

Deflation/Rupture/Leakage

Breast implants **are not lifetime devices** and cannot be expected to last forever. Some implants deflate or rupture in the first few months after being implanted and some deflate after several years; others are intact 10 or more years after the surgery.

a. Silicone Gel-Filled Breast Implants – When silicone gel-filled implants rupture, some women may notice decreased breast size, nodules (hard knots), uneven appearance of the breasts, pain or tenderness, tingling, swelling, numbness, burning, or changes in sensation.

Other women may unknowingly experience a rupture without any symptoms (i.e., “silent rupture”). Magnetic resonance imaging (MRI) with equipment specifically designed for imaging the breast may be used for evaluating patients with suspected rupture or leakage of their silicone gel-filled implant.

Silicone gel which escapes the fibrotic capsule surrounding the implant may migrate away from the breast. The free silicone may cause lumps called granulomas to form in the breast or other tissues where the silicone has migrated, such as the chest wall, armpit, arm, or abdomen.

Plastic surgeons usually recommend removal of the implant if it has ruptured, even if the silicone is still enclosed within the scar tissue capsule, because the silicone gel may eventually leak into surrounding tissues. If you are considering the removal of an implant and the implantation of another one, be sure to discuss the benefits and risks with your doctor.

FDA completed a retrospective study on rupture of silicone gel-filled breast implants.¹ This study was performed in Birmingham, Alabama and included women who had their first breast implant before 1988. Women with silicone gel-filled breast implants had a MRI examination of their breasts to determine the status of their current breast implants.

The 344 women who received a MRI examination had a total of 687 implants. Of the 687 implants in the study, at least two of the three study radiologists agreed that 378 implants were ruptured (55%). This means that 69% of the 344 women had at least one ruptured breast implant. Of the 344 women, 73 (21%) had extracapsular silicone gel in one or both breasts. Factors that were associated with rupture included increasing age of the implant, the implant manufacturer, and submuscular rather than subglandular location of the implant. A summary of the findings of this study is also available on FDA’s website at <http://www.fda.gov/cdrh/breastimplants/studies/biinterview.pdf> and

¹ Brown SL, Middleton MS, Berg WA, Soo MS, Pennello G. Prevalence of rupture of silicone gel breast implants in a population of women in Birmingham, Alabama. American Journal of Roentgenology 2000; 175:1-8

<http://www.fda.gov/cdrh/breastimplants/studies/birupture.pdf>

Robinson et al. studied 300 women who had their implants for 1 to 25 years and had them removed for a variety of reasons.² Visible signs of rupture in 51% of the women studied were found. Severe silicone leakage (silicone outside the implant without visible tears or holes) was seen in another 20%. Robinson et al. also noted that the chance of rupture increases as the implant ages.

Other studies indicate that silicone may escape the capsule in 11-23% of rupture cases.^{3,4,5,6}

For the Core Gel Study, a randomly selected subset of 405 patients will undergo MRI scans at 1, 2, 4, 6, 8, and 10 years. The purpose of this substudy is to determine the rate of silent rupture. Scans will be sent to a central reading center to be read by an independent breast MRI radiologist. This radiologist will be blinded to the patient name and site. The results will be entered into the study database. All patients, whether or not they are randomized to undergo MRI scans, will be directed to see their physician whenever the patient believes a rupture has occurred.

Gel Bleed: Silicone gel is made up of a sponge like mesh filled with silicone in oil form. This oil is used in many medical products such as syringes, pills and anti-gas medications such as Mylanta. It is known that some very small amounts of the oil part of the gel “bleeds” through the implant’s covering or envelope. Although most of this stays in the implant pocket or is trapped in the surrounding scar, minute amounts of this silicone could possibly travel (migrate) to different parts of the body.

Silicone oil has not been demonstrated to cause cancer or other illnesses.

Changes in Nipple and Breast Sensation/Breast Pain: Any surgery on the breast, including a biopsy or breast implant surgery, can result in the breast and/or nipple being oversensitive or undersensitive on one or both sides. This change can vary in degree and may be temporary or permanent. It may affect comfort while nursing or sexual response.

Most women undergoing augmentation or reconstruction with a mammary prosthesis will experience some breast and/or chest pain postoperatively. While this pain normally subsides in most women as they heal after surgery, it can become a chronic problem in other women.

¹ Robinson OG, Bradley EL, Wilson DS. Analysis of explanted silicone implants: a report of 300 patients. *Ann Plast Surg* 1995; 34:1-7.

³ Vinnik CA. Migratory silicone – clinical aspects. *Silicone in Medical Devices – Conference Proceedings* 1991 February 1-2, Baltimore, MD. U.S. Department of Health and Human Services, FDA Publication No. 92-4249 (p 59-67)

⁴ Duffy MJ, Woods JE. Health risks of failed silicone gel breast implants: a 30-year clinical experience. *Plast Reconstr Surg* 1994;94:295-299

⁵ Berg WA, Caskey CI, Hamper UM, Kuhlman JE, Anderson ND, Chang BW, Sheth S, Zerhouni EA. Single- and double-lumen silicone breast implant integrity: Prospective evaluation of MR and US criteria. *Radiology* 1995;197:45-52

⁶ Gorczyca DP, Schneider E, DeBruhl ND, Foo TKF, Ahn CY, Sayre JW, Shaw WW, Bassett LW. Silicone breast implant rupture. Comparison between three-point Dixon and fast spin-echo MR imaging. *AJR* 1994;162:305-310

Chronic pain can be associated with hematoma, migration, infection, and implants that are too large or capsular contracture. Sudden severe pain may be associated with implant rupture.

Interference with Mammography in Detection of Cancer: An implant may interfere with the detection of early breast cancer because it may “hide” suspicious lesions in the breast during an x-ray examination. It is especially important for women who are at high risk of developing breast cancer to consider this before having implants. The earlier cancer is detected, the better a chance for a cure.

Regular self-examination is very important for all women but especially if you have implants. You are urged to contact the American Cancer Society for literature and instructions on the early detection of cancer.

Since the breast is compressed during mammography, it is possible, but rare, for an implant to rupture. These problems can be reduced, but not eliminated, by asking if the personnel at the facility are experienced in performing mammography on women with implants. Before the mammography exam, you should tell the technologist that you have implants. The technologist should take special care when compressing the breast to avoid rupture. Also, an experienced technologist should know how to push the implant away from the breast tissue to get the best possible views of the tissue. Even when this special technique is used, some breast tissue may be missed in the x-ray. More x-ray views are necessary with these special techniques; therefore, women with breast implants will receive more radiation. However, the benefit of the mammogram in finding cancer outweighs the risk of the additional x-rays.

Calcium Deposits: Small spots of calcium in the breast are often found in any breast and can be seen on x-rays (mammography). These deposits may not occur in breasts with implants and may not appear for years after the implant surgery. They are benign (noncancerous) and cause no problems but must be differentiated from the calcium that is often seen in breast cancers. An expert radiologist can usually tell a benign (non-cancerous) calcium spot from a malignant one but occasionally a biopsy may be necessary to make this distinction. Some patients may develop a thin layer of calcium in the scar capsule that surrounds the implant. This is almost always associated with capsular contracture but otherwise causes no known problem.

Delayed Wound Healing: In some cases, the incision site fails to heal normally.

Extrusion: Unstable or compromised tissue covering and/or interruption of wound healing may result in extrusion, which is when the breast implant comes through the skin.

Necrosis: Necrosis is the formation of dead tissue around the implant. This may prevent wound healing and require surgical correction and/or implant removal. Permanent scar deformity may occur following necrosis. Factors associated with increased necrosis include infection, use of steroids in the surgical pocket, smoking, chemotherapy/radiation, and excessive heat or cold therapy.

Breast Tissue Atrophy/Chest Wall Deformity: The pressure of the breast implant may cause the breast tissue to thin and shrink. This can occur while implants are still in place or following implant removal without replacement.

Dissatisfaction with Cosmetic Results: You may not be satisfied with the appearance of your breasts after implants. The surgeon has only limited control over the final shape which is finally determined by how your chest, your breast and the implant all fit together. Incorrect implant size, excessive scarring and misplacement of implants may interfere with satisfactory appearance. Asymmetry (unequal breast size or shape) may not be totally corrected even by different sized implants. The implanted breast may sag or droop (ptosis) over time, much like a natural breast.

In addition, breast implants will not prevent your breast(s) from sagging after pregnancy. Very rarely the implant may change position or break through the skin, particularly if you have very thin breast tissue covering it. You may be able to feel or see wrinkles in the implant through your skin.

Granulomas: These are non-cancerous lumps that can form when certain body cells surround foreign material, such as silicone. Like any lump, it should be further evaluated to distinguish it from a lump that might be cancerous and require biopsy.

Resurgery: Whether you are undergoing augmentation or reconstruction, you should understand that there is a high chance that you will need to have additional surgery at some point to replace or remove the implant. Also, problems such as rupture, capsular contracture, infection, shifting, and calcium deposits can require removal of the implants. Many women decide to have the implants replaced, but some women do not. Those who do may have cosmetically unacceptable dimpling and/or puckering of the breast following removal of the implant.

10. UNKNOWN RISKS

The long-term biological effects of silicone compounds in women have received a great deal of attention over the last 25 years. Both rupture and gel bleed may result in silicone going to other parts of the body. Concerns have included connective tissue disease, immunological and neurological disorders, and the risk of cancer.

Connective Tissue Disorders: There have been reports describing an association between certain silicone-based products and certain connective tissue disorders. These are a group of disorders in which the body reacts to its own tissue as though it was foreign material. These disorders can cause long-term, serious, disabling health problems. Symptoms may include pain and swelling of joints, tightness, redness or swelling of the skin, swollen glands or lymph nodes, unusual and unexplained fatigue, swelling of the hands and feet, and unusual hair loss. Generally, people who have these relatively rare connective tissue disorders experience a combination of these and other symptoms.

Some cases of these disorders have been reported in women with breast implants. Some of these women have reported a reduction in symptoms after their implants were removed.

Neurological Symptoms: There have been some reports of patients experiencing neurological symptoms at variable times after breast implant surgery. Some of the complaints have involved difficulties with vision, sensation, muscle strength, walking, and balance.

Cancer: There is presently no established scientific evidence that links either silicone gel-filled or saline-filled breast implants with cancer. However, the possibility cannot be ruled out.

Birth Defects: Preliminary animal studies and a study in humans show no evidence that birth defects are caused by silicone implants. However, to rule out that possibility for humans, further scientific studies are necessary to show whether or not breast implants are associated with birth defects.

Breast feeding: Many women with breast implants have nursed their babies successfully. Any breast surgery, such as breast biopsy or partial mastectomy, that removes a great deal of breast tissue, or even breast implant surgery, could theoretically interfere with your ability to nurse your baby or the amount of milk available.

In recent years there has been some question as to whether small amounts of silicone that “bleeds” from gel-filled breast implants can find its way into breast milk, and, if this were to occur, could that affect the child. If you are considering breast-feeding, you are urged to check with your doctor or the FDA’s Breast Implant Information line at (800-532-4440) for the most current information. The American Academy of Pediatrics has stated that “there is no reason why a woman with implants should refrain from nursing.”

11. ALTERNATIVE PROCEDURES TO PARTICIPATION IN THIS STUDY

You may choose not to participate in this study. There are several alternative procedures to breast augmentation with silicone gel-filled breast implants. These include having nothing done or wearing an external prosthesis inside your bra. Breasts can be made by transferring fatty tissues from other parts of the body such as the stomach, buttock or back (flap procedure). For many women, saline-filled breast implants are also an alternative.

Your doctor will discuss these and other procedures and their relative risks and benefits.

12. IMPORTANT FACTORS TO CONSIDER WHEN DECIDING TO HAVE GEL-FILLED IMPLANTS

- Whether you are undergoing augmentation or reconstruction, be aware that breast implantation may not be a one time surgery. You are likely to need additional surgery and doctor visits over the course of your life.
- Breast implants are not considered lifetime devices. You will likely undergo implant removal with or without replacement over the course of your life.

- Many of the changes to your breast following implantation are irreversible (cannot be undone). If you later choose to have your implant(s) removed, you may experience unacceptable dimpling, puckering, wrinkling, or other cosmetic changes of the breast.
- Breast implants may affect your ability to produce milk for breast feeding. Also, breast implants will not prevent your breast from sagging after pregnancy.
- With breast implants, routine screening mammography will be more difficult, and you will need to have additional views, which means more time and radiation.
- For patients who have undergone breast implantation either as a cosmetic or a reconstructive procedure, health insurance premiums may increase, coverage may be dropped, and/or future coverage may be denied. Treatment of complications may not be covered as well. You should check with your insurance company regarding these coverage issues.

Augmentation - Insurance does not cover breast augmentation and may not cover reoperation (additional surgery) and additional doctor's visits following augmentation.

Reconstruction - Most insurance covers the first breast reconstruction operation. Insurance coverage for reoperation procedures or additional doctor's visits following reconstruction may not be covered, depending on the policy.

13. COSTS/FINANCIAL INCENTIVES

All costs incurred for this surgical procedure are between you and your doctor(s), including the cost of standard visits and any additional procedures or visits to another specialist that may be required for the operation. If, during the course of the study, you exhibit signs of a rheumatological condition, you will be referred to a rheumatologist for an evaluation at Mentor's expense. Mentor will also pay for the MRI examinations if you are in the group required to undergo MRI procedures, or if you are suspected of having a ruptured implant.

Mentor will provide to you installment payments that may assist with costs incurred as a result of your participation in this Study. Incentive checks will be made out in your name and mailed directly to your home. You will be paid after the completion of the following post-operative visits:

Payment	Visit	Payment	Visit
	Implantation		5 year visit
	6 month visit		6 year visit
	12 month visit		7 year visit
	24 month visit		8 year visit
	Bonus if no visits are missed through 24 months		9 year visit
	3 year visit		10 year visit
	4 year visit		Bonus if no visits are missed through 10 years (all 11 postoperative visits)
Total incentives for all visits			
Total incentive with no missed postoperative visits			

14. COMPENSATION FOR INJURY

Compensation for physical injuries, complications or medical treatment from your participation in this study is not available from Mentor other than outlined in the attached Mentor Warranty. If your complication is related to rupture, you will be reimbursed under the warranty policy. If a problem occurs, medical treatment will continue to be available. Your doctor will let you know what to do if you experience any complications while you are in this Study.

15. CONFIDENTIALITY

Your confidentiality will be protected as much as possible throughout this study. Records generated during this study which identify you by name will be maintained as confidential, with the exception that those records, as well as your medical records, may be reviewed by authorized representatives from your doctor's office and from Mentor. In addition, authorized representatives from the U.S. Food and Drug Administration may inspect the records. Results of data collected will be reported as numbers only, no names. Under certain circumstances, your clinical records could be obtained by Congress or a court order. While every effort will be taken to keep this information confidential, under these special circumstances, this could mean public disclosure of your surgery and loss of your privacy.

16. LEGAL RISK AND ANALYSIS OF REMOVED IMPLANT

If your implant needs to be removed, Mentor requests the implant be returned to Product Evaluation to be analyzed. This could have implications in any legal action involving your implant. Mentor will ask your permission to analyze it, a process that may alter or destroy it. You will be contacted first through your doctor and asked whether you wish to give permission for such an evaluation. Results of the analysis will be made available to you, your doctor and/or the FDA upon request. Mentor and the FDA believe there is scientific benefit to testing an explanted implant

17. QUESTIONS

During the course of the study, you will be informed by your doctor regarding any new information about Mentor Round Low-Bleed Silicone Gel-filled Mammary Prostheses, which may become known during the study. You also have the right to ask questions and have them answered.

For questions about your procedure and any research related injury, you should contact your doctor, Dr. _____ at () _____.

For questions regarding your participation in the Study and your rights as a research patient, please contact the local, national, or non-local independent reviewer of the research listed below:

Western Institutional Review Board (WIRB)
3535 7th Ave., NW
Olympia, Washington 98502
206-943-1410 FAX 206-943-4522

18. VOLUNTARY PARTICIPATION AND WITHDRAWAL FROM STUDY

Your participation in this Study is voluntary and your decision not to participate will not result in loss of benefits to which you are otherwise entitled; however, you will not receive Mentor Round Low-Bleed Silicone Gel-filled Mammary Prostheses without being in this Study. You may drop out at any time and you will still receive all necessary medical care.

19. ACKNOWLEDGEMENT

I was provided this Informed Consent in advance and met with my doctor, to discuss the information. All my questions have been answered to my satisfaction and I have been provided a copy of this Informed Consent and the Experimental Patient's Bill of Rights (in California only).

Patient/Patient's Signature

Date

Patient/Patient's Printed Name

Signature of Person Obtaining Consent

Date

Warranty Summary for Mentor Round Low-Bleed Silicone Gel-filled Mammary Prostheses

A. What Does the Warranty Cover?

The warranty covers patients' uninsured, out-of-pocket costs that are directly related to breast implant revision surgery. When the warranty applies, Mentor provides the following:

- **Free Lifetime Replacement:** Throughout a patient's lifetime Mentor will replace, at no cost, the same or a similar type of Mentor breast implant when implant replacement is required. If a more expensive product is requested, Mentor will invoice the surgeon for the price difference.
- **Financial Assistance:** For the first five years following a breast implant procedure, Mentor will provide financial assistance up to \$████, per revision surgery to help cover operating room expenses and anesthesia expenses not covered by insurance.

B. What Products are covered?

The Mentor breast implant warranty automatically applies to Mentor Round Low-Bleed Silicone Gel-filled Mammary Prostheses that are implanted as part of the this Study, provided these implants have been:

- Implanted in accordance with Mentor literature, current to the date of implantation, and other notifications or instructions published by Mentor.
- Used by appropriately qualified, licensed surgeons, in accordance with accepted surgical procedures.

C. What Events are Covered?

This Mentor breast implant warranty applies to rupture of any all Mentor Round Low-Bleed Silicone Gel-filled Mammary Prostheses.

Other loss-of-shell integrity events also may be covered by this warranty. A physician retained by Mentor will determine if specific, additional events should be covered. However, events listed in section D of this brochure will not be covered.

D. What Events are Not Covered?

The Mentor breast implant warranty does not cover the following:

- Removal of intact implants due to capsular contracture, wrinkling or rippling.
- Loss of implant shell integrity resulting from reoperative procedures, open capsulotomy, or closed compression capsulotomy procedures.
- Removal of intact implants for size alteration.

E. How are Claims Filed?

To file a warranty claim for covered events, the surgeon must contact Mentor's Consumer Affairs Department.

Warranty Summary for Mentor Round Low-Bleed Silicone Gel-filled Mammary Prostheses

- When necessary materials from the surgeon are received and confirmed by Mentor, replacement product(s) and/or a check will be issued to the appropriate party in accordance with Mentor's warranty.
- Prior to reimbursement for revision surgery, the surgeon must complete all forms and requested documentation about medical treatments and expenses

ATTACHMENT 4
BAKER CLASSIFICATION GRADING SCALE

BAKER CLASSIFICATION GRADING SCALE

Class	Description
1	The breast feels as soft as an unoperated one and the implant cannot be palpated.
2	The breast is less soft; the implant can be palpated but it is not visible.
3	The breast is more firm; the implant can be easily palpated and it (or distortion from it) can be seen.
4	The breast is hard, tender, painful, cold and distortion is often marked.

ATTACHMENT 5
QUALITY OF LIFE QUESTIONNAIRES



Core Gel Breast
IDE Clinical Trial

BASELINE

PATIENT STUDY ID:

TRIAL NO
10-009

COUNTRY NO
0 | 0 | 1

SITE NO

PATIENT NO

PATIENT INITIALS
first middle last

ROSENBERG SELF-ESTEEM SCALE (Page 1 of 1)

TO THE PATIENT: Below are some statements with which some people agree and disagree. Please read each statement and check **one** response to each statement.

	Strongly Agree 1	Agree 2	Disagree 3	Strongly Disagree 4
1. I feel that I am a person of worth, at least on an equal basis with others.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
2. I feel that I have a number of good qualities.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3. All in all, I am inclined to feel that I am a failure.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
4. I am able to do things as well as most people.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
5. I feel I do not have much of which to be proud.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
6. I take a positive attitude towards myself.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
7. On the whole, I am satisfied with myself.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
8. I wish I could have more respect for myself.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
9. I certainly feel useless at times.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
10. At times I think I am no good at all.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>



**Core Gel Breast
IDE Clinical Trial**

BASELINE

PATIENT STUDY ID:

TRIAL NO
10-009

COUNTRY NO
0 | 0 | 1

SITE NO

PATIENT NO

PATIENT INITIALS
first middle last

TENNESSEE SELF-CONCEPT SCALE (Page 1 of 4)

TO THE PATIENT: The statements below are to help you describe yourself as you see yourself. Please respond to them as if you were describing yourself **to yourself**. Do not omit any item. Read each statement carefully, then select one of the five responses listed below. On the test, put a **circle** around the response you chose. If you want to change an answer after you have circled it, do not erase it but put an X mark through the response and then circle the response you want.

<i>Remember, put a circle around the response number you have chosen for each statement.</i>	Completely False	Mostly False	Partly True and Partly False	Mostly True	Completely True
1. I have a healthy body.	1	2	3	4	5
2. I am an attractive person.	1	2	3	4	5
3. I consider myself a sloppy person.	1	2	3	4	5
4. I am a decent sort of person.	1	2	3	4	5
5. I am an honest person.	1	2	3	4	5
6. I am a bad person.	1	2	3	4	5
7. I am a cheerful person.	1	2	3	4	5
8. I am a calm and easygoing person.	1	2	3	4	5
9. I am a nobody.	1	2	3	4	5
10. I have a family that would always help me in any kind of trouble.	1	2	3	4	5
11. I am a member of a happy family.	1	2	3	4	5
12. My friends have no confidence in me.	1	2	3	4	5
13. I am a friendly person.	1	2	3	4	5
14. I am popular with men.	1	2	3	4	5
15. I am not interested in what other people do.	1	2	3	4	5
16. I do not always tell the truth.	1	2	3	4	5
17. I get angry sometimes.	1	2	3	4	5
18. I like to look nice and neat all the time.	1	2	3	4	5
19. I am full of aches and pains.	1	2	3	4	5
20. I am a sick person.	1	2	3	4	5
21. I am a religious person.	1	2	3	4	5
22. I am a moral failure.	1	2	3	4	5
23. I am a morally weak person.	1	2	3	4	5

 MENTOR	Core Gel Breast IDE Clinical Trial			BASELINE							
	PATIENT STUDY ID:	TRIAL NO 10-009	COUNTRY NO 0 0 1			SITE NO		PATIENT NO		PATIENT INITIALS first middle last	

TENNESSEE SELF-CONCEPT SCALE (Page 2 of 4)

<i>Remember, put a circle around the response number you have chosen for each statement.</i>	Completely False	Mostly False	Partly True and Partly False	Mostly True	Completely True
24. I have a lot of self-control.	1	2	3	4	5
25. I am a hateful person.	1	2	3	4	5
26. I am losing my mind.	1	2	3	4	5
27. I am an important person to my friends and family.	1	2	3	4	5
28. I am not loved by my family.	1	2	3	4	5
29. I feel that my family doesn't trust me.	1	2	3	4	5
30. I am popular with women.	1	2	3	4	5
31. I am mad at the whole world.	1	2	3	4	5
32. I am hard to be friendly with.	1	2	3	4	5
33. Once in a while I think of things too bad to talk about.	1	2	3	4	5
34. Sometimes when I am not feeling well, I am cross.	1	2	3	4	5
35. I am neither too fat nor too thin.	1	2	3	4	5
36. I like my looks just the way they are.	1	2	3	4	5
37. I would like to change some parts of my body.	1	2	3	4	5
38. I am satisfied with my moral behavior.	1	2	3	4	5
39. I am satisfied with my relationship to God.	1	2	3	4	5
40. I ought to go to church more.	1	2	3	4	5
41. I am satisfied to be just what I am.	1	2	3	4	5
42. I am just as nice as I should be.	1	2	3	4	5
43. I despise myself.	1	2	3	4	5
44. I am satisfied with my family relationships.	1	2	3	4	5
45. I understand my family as well as I should.	1	2	3	4	5
46. I should trust my family more.	1	2	3	4	5
47. I am as sociable as I want to be.	1	2	3	4	5
48. I try to please others, but I don't overdo it	1	2	3	4	5
49. I am no good at all from a social standpoint.	1	2	3	4	5

 MENTOR	Core Gel Breast IDE Clinical Trial			BASELINE							
	PATIENT STUDY ID:	TRIAL NO 10-009	COUNTRY NO 0 0 1			SITE NO		PATIENT NO		PATIENT INITIALS first middle last	

TENNESSEE SELF-CONCEPT SCALE (Page 3 of 4)

<i>Remember, put a circle around the response number you have chosen for each statement.</i>	Completely False	Mostly False	Partly True and Partly False	Mostly True	Completely True
50 I do not like everyone I know.	1	2	3	4	5
51 Once in a while, I laugh at a dirty joke.	1	2	3	4	5
52 I am neither too tall nor too short.	1	2	3	4	5
53 I don't feel as well as I should.	1	2	3	4	5
54 I should have more sex appeal.	1	2	3	4	5
55 I am as religious as I want to be.	1	2	3	4	5
56. I wish I could be more trustworthy.	1	2	3	4	5
57. I shouldn't tell so many lies.	1	2	3	4	5
58. I am as smart as I want to be.	1	2	3	4	5
59 I am not the person I would like to be.	1	2	3	4	5
60 I wish I didn't give up as easily as I do.	1	2	3	4	5
61. I treat my parents as well as I should. <i>(Use past tense if parents are not living)</i>	1	2	3	4	5
62. I am too sensitive to things my family says.	1	2	3	4	5
63. I should love my family more.	1	2	3	4	5
64. I am satisfied with the way I treat other people.	1	2	3	4	5
65 I should be more polite to others.	1	2	3	4	5
66 I ought to get along better with other people.	1	2	3	4	5
67. I gossip a little at times.	1	2	3	4	5
68. At times I feel like swearing.	1	2	3	4	5
69. I take good care of myself physically.	1	2	3	4	5
70. I try to be careful about my appearance.	1	2	3	4	5
71. I often act like I am "all thumbs".	1	2	3	4	5
72. I am true to my religion in my everyday life.	1	2	3	4	5
73. I try to change when I know I'm doing things that are wrong.	1	2	3	4	5
74. I sometimes do very bad things.	1	2	3	4	5
75. I can always take care of myself in any situation.	1	2	3	4	5

 MENTOR	Core Gel Breast IDE Clinical Trial			BASELINE						
	PATIENT STUDY ID:	TRIAL NO 10-009	COUNTRY NO 0 0 1			SITE NO		PATIENT NO		PATIENT INITIALS first middle last

TENNESSEE SELF-CONCEPT SCALE (Page 4 of 4)

<i>Remember, put a circle around the response number you have chosen for each statement.</i>	Completely False	Mostly False	Partly True and Partly False	Mostly True	Completely True
76. I take the blame for things without getting mad.	1	2	3	4	5
77. I do things without thinking about them first.	1	2	3	4	5
78. I try to play fair with my friends and family.	1	2	3	4	5
79. I take a real interest in my family.	1	2	3	4	5
80. I give in to my parents. <i>(Use past tense if parents are not living.)</i>	1	2	3	4	5
81. I try to understand the other fellow's point of view.	1	2	3	4	5
82. I get along well with other people.	1	2	3	4	5
83. I do not forgive others easily.	1	2	3	4	5
84. I would rather win than lose in a game.	1	2	3	4	5
85. I feel good most of the time.	1	2	3	4	5
86. I do poorly in sports and games.	1	2	3	4	5
87. I am a poor sleeper.	1	2	3	4	5
88. I do what is right most of the time.	1	2	3	4	5
89. I sometimes use unfair means to get ahead.	1	2	3	4	5
90. I have trouble doing the things that are right.	1	2	3	4	5
91. I solve my problems quite easily.	1	2	3	4	5
92. I change my mind a lot.	1	2	3	4	5
93. I try to run away from my problems.	1	2	3	4	5
94. I do my share of work at home.	1	2	3	4	5
95. I quarrel with my family.	1	2	3	4	5
96. I do not act like my family thinks I should.	1	2	3	4	5
97. I see good points in all the people I meet.	1	2	3	4	5
98. I do not feel at ease with other people.	1	2	3	4	5
99. I find it hard to talk with strangers.	1	2	3	4	5
100. Once in a while I put off until tomorrow what I ought to do today.	1	2	3	4	5



MENTOR

**Core Gel Breast
IDE Clinical Trial**

BASELINE

PATIENT STUDY ID:

TRIAL NO
10-009

COUNTRY NO
0 | 0 | 1

SITE NO

PATIENT NO

PATIENT INITIALS
first middle last

SF-36 (Page 1 of 3)

TO THE PATIENT: This survey asks for your views about your health. This information will help keep track of how you feel and how well you are able to do your usual activities.

Answer each question by circling **one** number. If you are unsure about how to answer a question, please give the best answer you can.

1. In general, would you say your health is: (Circle one number)	Excellent	Very Good	Good	Fair	Poor
	1	2	3	4	5

2. Compared to one year ago, how would you rate your health in general now ? (Circle one number)	Much Better Now	Somewhat Better Now	About the Same	Somewhat Worse Now	Much Worse Now
	1	2	3	4	5

3. The following questions are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much? (Circle one number for each question.)	Yes, Limited a Lot	Yes, Limited a Little	No, Not Limited at All
Vigorous activities , such as running, lifting heavy objects, participating in strenuous sports.	1	2	3
Moderate activities , such as moving a table, pushing a vacuum cleaner, bowling or playing golf	1	2	3
Lifting or carrying groceries	1	2	3
Climbing several flights of stairs	1	2	3
Climbing one flight of stairs	1	2	3
Bending, kneeling, or stooping	1	2	3
Walking more than a mile	1	2	3
Walking several blocks	1	2	3
Walking one block	1	2	3
Bathing or dressing yourself	1	2	3



**Core Gel Breast
IDE Clinical Trial**

BASELINE

PATIENT STUDY ID:	TRIAL NO	COUNTRY NO			SITE NO			PATIENT NO			PATIENT INITIALS		
	10-009	0	0	1							first	middle	last

SF-36 (Page 2 of 3)

4. During the past 4 weeks , have you had any of the following problems with your work or other regular daily activities as a result of your physical health? (Circle one number for each question.)	YES	NO
Cut down on the amount of time you spent on work or other activities	1	2
Accomplished less than you would like	1	2
Were limited in the kind of work or other activities	1	2
Had difficulty performing the work or other activities (for example, it took extra effort)	1	2

5. During the past 4 weeks , have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (such as feeling depressed or anxious)? (Circle one number for each question.)	YES	NO
Cut down on the amount of time you spent on work or other activities	1	2
Accomplished less than you would like	1	2
Didn't do work or other activities as carefully as usual	1	2

6. During the past 4 weeks , to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbors, or groups? (Circle one number)	Not at All	Slightly	Moderately	Quite a Bit	Extremely
	1	2	3	4	5

7. How much bodily pain have you had during the past 4 weeks? (Circle one number)	None	Very Mild	Mild	Moderate	Severe	Very Severe
	1	2	3	4	5	6

8. During the past 4 weeks , how much did pain interfere with your normal work (including both work outside the home and housework)? (Circle one number)	Not at All	A Little Bit	Moderately	Quite a Bit	Extremely
	1	2	3	4	5

**MENTOR****Core Gel Breast
IDE Clinical Trial****BASELINE****PATIENT STUDY ID:**TRIAL NO
10-009COUNTRY NO
0 | 0 | 1

SITE NO

PATIENT NO

PATIENT INITIALS
first middle last**SF-36 (Page 3 of 3)**

9. These questions are about how you feel and how things have been with you **during the past 4 weeks**. For each question, please indicate the one answer that comes closest to the way you have been feeling. (Circle **one** number for each question.)

How much of the time during the past 4 weeks ...	All of the Time	Most of the Time	A Good Bit of the Time	Some of the Time	A Little of the Time	None of the Time
Did you feel full of pep?	1	2	3	4	5	6
Have you been a very nervous person?	1	2	3	4	5	6
Have you felt so down in the dumps that nothing could cheer you up?	1	2	3	4	5	6
Have you felt calm and peaceful?	1	2	3	4	5	6
Did you have a lot of energy?	1	2	3	4	5	6
Have you felt downhearted and blue?	1	2	3	4	5	6
Did you feel worn out?	1	2	3	4	5	6
Have you been a happy person?	1	2	3	4	5	6
Did you feel tired?	1	2	3	4	5	6

10 During the past 4 weeks , how much of the time has your physical health or emotional problems interfered with your social activities (like visiting with friends, relatives, etc.)? (Circle one number.)	All of the Time	Most of the Time	Some of the Time	A Little of the Time	None of the Time
	1	2	3	4	5

11. How TRUE or FALSE is each of the following statements for you? (Circle one number for each question.)	Definitely True	Mostly True	Don't Know	Mostly False	Definitely False
I seem to get sick a little easier than other people	1	2	3	4	5
I am as healthy as anybody I know	1	2	3	4	5
I expect my health to get worse	1	2	3	4	5
My health is excellent	1	2	3	4	5



**Core Gel Breast
IDE Clinical Trial**

BASELINE

PATIENT STUDY ID:

TRIAL NO
10-009

COUNTRY NO
0 | 0 | 1

SITE NO

PATIENT NO

PATIENT INITIALS
first middle last

BODY ESTEEM SCALE (Page 1 of 1)

TO THE PATIENT: On this page are listed a number of body parts and functions. Please read each item and indicate how you feel about this part or function of ***your own body***, using the following scale:

- 1 = Have strong negative feelings
- 2 = Have moderate negative feelings
- 3 = Have no feeling one way or the other
- 4 = Have moderate positive feelings
- 5 = Have strong positive feelings

- | | |
|--|--|
| <input type="checkbox"/> 1. Body Scent | <input type="checkbox"/> 19. Arms |
| <input type="checkbox"/> 2. Appetite | <input type="checkbox"/> 20. Chest |
| <input type="checkbox"/> 3. Nose | <input type="checkbox"/> 21. Appearance of Eyes |
| <input type="checkbox"/> 4. Physical Stamina | <input type="checkbox"/> 22. Cheeks/Cheekbones |
| <input type="checkbox"/> 5. Reflexes | <input type="checkbox"/> 23. Hips |
| <input type="checkbox"/> 6. Lips | <input type="checkbox"/> 24. Legs |
| <input type="checkbox"/> 7. Muscular Strength | <input type="checkbox"/> 25. Physique |
| <input type="checkbox"/> 8. Waist | <input type="checkbox"/> 26. Sex Drive |
| <input type="checkbox"/> 9. Energy Level | <input type="checkbox"/> 27. Feet |
| <input type="checkbox"/> 10. Thighs | <input type="checkbox"/> 28. Sex Organs |
| <input type="checkbox"/> 11. Ears | <input type="checkbox"/> 29. Appearance of Stomach |
| <input type="checkbox"/> 12. Biceps | <input type="checkbox"/> 30. Health |
| <input type="checkbox"/> 13. Chin | <input type="checkbox"/> 31. Sex Activities |
| <input type="checkbox"/> 14. Body Build | <input type="checkbox"/> 32. Body Hair |
| <input type="checkbox"/> 15. Physical Coordination | <input type="checkbox"/> 33. Physical Condition |
| <input type="checkbox"/> 16. Buttocks | <input type="checkbox"/> 34. Face |
| <input type="checkbox"/> 17. Agility | <input type="checkbox"/> 35. Weight |
| <input type="checkbox"/> 18. Width of Shoulders | |



Core Gel Breast
IDE Clinical Trial

BASELINE

PATIENT STUDY ID:

TRIAL NO
10-009

COUNTRY NO
0 0 1

SITE NO

PATIENT NO

PATIENT INITIALS
first middle last

MANITOBA CANCER TREATMENT & RESEARCH FOUNDATION FUNCTIONAL LIVING INDEX: CANCER (FLIC)

Page 1 of 3

N/A (not a cancer patient)

TO THE PATIENT: Please indicate your rating by drawing a vertical line (|).

1. Most people experience some feelings of depression at times. Rate how often you feel these feelings.

1	2	3	4	5	6	7
Never						Continually

2. How well are you coping with your everyday stress?

1	2	3	4	5	6	7
Not Well						Very Well

3. How much time do you spend thinking about your illness?

1	2	3	4	5	6	7
Constantly						Never

4. Rate your ability to maintain your usual recreation or leisure activities.

1	2	3	4	5	6	7
Able						Unable

5. Has nausea affected your daily functioning?

1	2	3	4	5	6	7
Not At All						A Great Deal

6. How well do you feel today?

1	2	3	4	5	6	7
Extremely Poor						Extremely Well

7. Do you feel well enough to make a meal or do minor household repairs today?

1	2	3	4	5	6	7
Very Able						Not Able



Core Gel Breast
IDE Clinical Trial

BASELINE

PATIENT STUDY ID:

TRIAL NO
10-009

COUNTRY NO
0 | 0 | 1

SITE NO

PATIENT NO

PATIENT INITIALS
first middle last

MANITOBA CANCER TREATMENT & RESEARCH FOUNDATION FUNCTIONAL LIVING INDEX: CANCER (FLIC)

Page 2 of 3

N/A (not a cancer patient)

8. Rate the degree to which your cancer has imposed a hardship on those closest to you in the past 2 months.

1	2	3	4	5	6	7
No Hardship			Tremendous Hardship			

9. Rate how often you feel discouraged about your life.

1	2	3	4	5	6	7
Always		Never				

10. Rate your satisfaction with your work and your jobs around the house in the past month.

1	2	3	4	5	6	7
Very Dissatisfied			Very Satisfied			

11. How uncomfortable do you feel today?

1	2	3	4	5	6	7
Not at All			Very Uncomfortable			

12. Rate in your opinion, how disruptive your cancer has been to those closest to you in the past 2 weeks.

1	2	3	4	5	6	7
Totally Disruptive			No Disruption			

13. How much is pain or discomfort interfering with your daily activities?

1	2	3	4	5	6	7
Not at All			A Great Deal			

14. Rate the degree to which your cancer has imposed a hardship on you (personally) in the past 2 weeks.

1	2	3	4	5	6	7
Tremendous Hardship			No Hardship			



MENTOR

**Core Gel Breast
IDE Clinical Trial**

BASELINE

PATIENT STUDY ID:

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10-009

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0 | 0 | 1

SITE NO

PATIENT NO

PATIENT INITIALS
first middle last

MANITOBA CANCER TREATMENT & RESEARCH FOUNDATION FUNCTIONAL LIVING INDEX: CANCER (FLIC)

Page 3 of 3

N/A (not a cancer patient)

15. How much of your usual household tasks are you able to complete?

1	2	3	4	5	6	7
All						None

16. Rate how willing you were to see and spend time with those closest to you, in the past 2 weeks.

1	2	3	4	5	6	7
Unwilling						Very Willing

17. How much nausea have you had in the past 2 weeks?

1	2	3	4	5	6	7
None						A Great Deal

18. Rate the degree to which you are frightened of the future.

1	2	3	4	5	6	7
Constantly Terrified						Not Afraid

19. Rate how willing you were to see and spend time with friends, in the past 2 weeks.

1	2	3	4	5	6	7
Unwilling						Very Willing

20. How much of your pain or discomfort over the past 2 weeks was related to your cancer?

1	2	3	4	5	6	7
None						All

21. Rate your confidence in your prescribed course of treatment.

1	2	3	4	5	6	7
No Confidence						Very Confident

22. How well do you appear today?

1	2	3	4	5	6	7
Extremely Poor						Extremely Well

**ATTACHMENT 6
INVESTIGATOR AGREEMENT**

Investigator Agreement

Core Gel Study of the Safety and Effectiveness of Mentor Round Low-Bleed Silicone Gel-filled Mammary Prostheses in Patients who are Undergoing Primary Breast Augmentation, Primary Breast Reconstruction or Revision (Core Gel Study)

Sponsor: Mentor, 201 Mentor Drive, Santa Barbara, CA USA 93111

Investigator:

This Investigator Agreement ("Agreement") is entered into as of _____, 200____, by and between _____ ("Investigator") and Mentor Corporation, a Minnesota corporation ("Sponsor").

1. Clinical Trial Requirements. Investigator's participation in the Core Gel Study of the Safety and Effectiveness of Mentor Round Low-Bleed Silicone Gel-filled Mammary Prostheses in Patients who are Undergoing Primary Breast Augmentation, Primary Breast Reconstruction or Revision (the "Trial") is conditioned upon the following representations and warranties made by the Investigator to the Sponsor:

- a) The Investigator assumes full responsibility for the trial, and agrees to conduct the investigation in accordance with applicable FDA regulations, conditions of approval imposed by the reviewing IRB or FDA, this Agreement, and the protocol, with which Investigator has been provided a copy and which Investigator fully understands.
- b) The Investigator assumes full responsibility for all actions taken by the Investigator or his/her staff in conducting the trial.
- c) Supervise all testing of the device involving human subjects.
- d) The Investigator states he/she is qualified to implant breast prosthesis.
- e) Investigator shall provide Sponsor with a current copy of Investigator's *curriculum vitae* (CV) to be accompanied with this Agreement. The CV will provide history on the Investigator's relevant experience.
- f) If the Investigator was involved in an investigation or other research that was terminated, an explanation of the circumstances that led to termination.
- g) Investigator shall prepare and maintain adequate case histories designed to record all observations and other data pertinent to the Trial and as requested by Sponsor. Adequate case histories, for purposes of this Trial, include all Case Report Forms as specified in the Trial protocol and required for Trial follow-up. Originals or photocopies of additional specialty consultation reports and other clinical support data generated on subjects enrolled as Trial subjects shall be provided to Sponsor upon request. The Case Report Forms remain the property of the Sponsor.

- h) Investigator shall furnish Investigator's reports to Sponsor in a timely manner. Specifically, documentation will be submitted as specified in the Trial protocol. Documentation not specifically listed in the Trial protocol (e.g., clinical support documentation as specified) will be maintained in subject case files for a period of five years after conclusion of the Trial and submitted to Sponsor upon request.
- i) The Investigator shall immediately report any death, serious injury or malfunction of the studied devices which could lead to a death or serious injury, to the Sponsor. Investigator acknowledges that such reports are required routinely for all medical devices as part of Sponsor's Product Evaluation department and federal regulations on Medical Device Reporting (MDR), and are not unique to this Trial. Reportable events include but are not limited to medical complications and events which are life threatening or may cause permanent impairment to Trial subjects.
- j) Investigator certifies that Investigator shall inform all potential Trial subjects that the device is being used in a clinical trial. The Investigator will enroll all subjects who meet the Inclusion/Exclusion Criteria, where the subject agrees to participate in the trial. The Investigator will obtain written Informed Consent from the subjects before surgery using the Informed Consent included in the Trial protocol, and will provide the subjects with a copy of their signed Informed Consent before surgery. In addition to the Informed Consent, the Investigator will explain the procedures to the subjects and will answer the subject's questions to the best of his/her ability.
- k) All information entered onto the Case Report Forms on Investigator subjects shall be correct and consistent with the subjects' medical records.
- l) Investigator shall obtain Institutional Review Board (IRB) approval and follow any additional terms which may be required by the IRB responsible for monitoring Investigator's participation in the Trial. Investigator shall not use the breast implant in Trial subjects until written IRB approval has been obtained. A copy of the IRB approval letter must be submitted to the Sponsor prior to Trial participation. Investigator shall maintain IRB approval during the duration of the Trial.
- m) Investigator understands that the Trial is subject to audit by the Food and Drug Administration (FDA) and Investigator shall allow access to subject files and documentation accumulated during the Trial to FDA officials.
- n) Investigator shall permit a representative of the Sponsor to make regular site visits during the course of the trial. The Investigator shall also permit the sponsor to inspect all Case Report Forms and corresponding portions of the Trial subject's medical records and source documents at regular intervals during the course of the Trial. The Investigator shall be available to meet with the Sponsor to discuss Trial progress, document and sign off on corrections, respond to questions and attest to completeness and accuracy of Case Report Forms and other requested information.

- o) Investigator shall follow all procedural instructions in the Product Insert Data Sheet, especially as noted in the "CONTRAINDICATIONS" "WARNINGS" sections of the insert.
- p) Investigator shall protect the privacy of Trial subjects to the extent possible and ensure that case trial documentation is kept secure at all times. Investigator shall promptly report any compromise in privacy to Sponsor and to Investigator's IRB.
- q) Investigator shall disclose sufficient and accurate financial disclosure information to allow the Sponsor to submit a complete and accurate disclosure statement. The Investigator will promptly update this information if any relevant changes occur during the course of the investigation and for one year following completion of the study.
- r) Investigator is not under any preexisting obligations inconsistent with the provisions of this agreement.

2. Confidentiality. Sponsor has disclosed or plans to disclose to Investigator certain confidential and proprietary information regarding its business and products, and specifically, information pertaining to the Trial ("Confidential Information"). Confidential information includes data gathered by Investigator as a result of participating in the trial. Mentor regards this information as confidential and requires that it remain secret. Investigator agrees that Investigator will:

- a) Hold all Confidential Information it receives from Sponsor in strict confidence and with the same degree of care that he/she gives to his/her own proprietary and confidential information, but not less than a reasonable degree of care, and not disclose such Confidential Information to others, except as may be required by law;
- b) Not use Confidential Information commercially or for any other purpose except to participate in the trial;
- c) Limit the dissemination of and access to Confidential Information to those personnel who have a need for access to such Confidential Information for Trial purposes and who are under an obligation of confidence consistent with this Agreement;
- d) Not copy or reproduce any records containing Confidential Information or divulge such records to others;
- e) Not disclose to others that Confidential Information is known to or used by Sponsor or those associated with Sponsor; and
- f) Return to Sponsor, within 30 calendar days of its written request or upon termination of this Agreement, all Confidential Information and any other records containing Confidential Information.

2.1 Inventions. All inventions reasonably related to the business of Sponsor's products or to any research, design, experiment, or production carried on by Sponsor, or to any matters specifically discussed with Investigator, including but not limited to improvements to products manufactured by Sponsor and research and development ideas or inventions of Sponsor, whether conceived, generated, or reduced to practice by Investigator alone or in conjunction with others, during the period of this Agreement or within a period of up to six months following this Agreement ("Inventions"), are the sole property of Sponsor and are hereby assigned to Sponsor. For purposes of this Agreement, inventions upon which Investigator files patent applications or enters into license or other agreements, within one year after termination of this Agreement shall be presumed to be Inventions as defined in this paragraph 2.1 and conceived by Investigator during the term of this Agreement and from consultations and discussions with Sponsor, subject to proof to the contrary in good faith, and written and duly corroborated records establishing that such invention or discovery was conceived and made by Investigator without the benefit of Investigator's relationship with Sponsor.

2.2 Assistance. Further, Investigator will give Sponsor all assistance Sponsor reasonably requires to perfect, protect, and use its rights to Inventions. In particular, without limitation, Investigator will sign all documents, do all things, and supply all information that Sponsor may deem necessary or desirable to (i) transfer or record the transfer of Investigator's entire right, title, and interest in Inventions and (ii) enable Sponsor to obtain patent, copyright, and trademark protection for Inventions anywhere in the world. The obligations of this paragraph 2.2 shall continue beyond the termination of this Agreement with respect to Inventions, discoveries, and improvements, whether patentable or not, conceived or made by Investigator during the term of this Agreement and shall be binding upon Investigator's assigns, executors, administrators and other legal representatives.

3. Subject Advertising. Subject advertisement is any notice, flyer, or brochure used to recruit subjects into a clinical trial. All advertisement for subject recruitment in clinical trials requires IRB approval prior to publication and copies of all proposed ads must be submitted to the Sponsor for prior approval.

4. Compensation. Sponsor shall compensate Investigator and the Investigator's Study Coordinator for participation in the Trial as set forth in Attachments A and B.

5. Amendment. All amendments or modifications of this Agreement shall be in writing and shall be signed by each of the parties hereto.

6. Waiver. Any waiver of any right, power, or privilege hereunder must be in writing and signed by the party being charged with the waiver. No delay on the part of any party hereto in exercising any right, power, or privilege hereunder shall operate as a waiver of any other right, power, or privilege hereunder, nor shall any single or partial exercise of any right, power, or privilege hereunder preclude any other or further exercise thereof or the exercise of any other right, power, or privilege.

7. Notices. All notices or other communications required or permitted to be given pursuant to this Agreement shall be in writing and shall be delivered personally or sent by overnight courier, by facsimile with confirmation by first-class mail, or by registered or certified mail, return receipt requested. Notices delivered personally or sent by overnight courier or by facsimile with confirmation by first-class mail shall be deemed to have been received and to be effective on the date received. While notices sent by registered or certified mail, return receipt requested, shall be deemed to have been received and to be effective three business days after deposit into the mails. Notices shall be given to the parties at the following respective addresses, or to such other addresses as any party shall designate in writing:

If to Sponsor: Mentor
Clinical Programs Department
201 Mentor Drive
Santa Barbara, CA 93111
Telephone: (805) 879-6000
Facsimile: (805) 879-6095

With a copy to: Legal Department
Mentor
201 Mentor Drive
Santa Barbara, California 93111
Telephone: (805) 879-6000
Facsimile: (805) 879-6006

If to the Investigator: _____

8. Successors and Assigns. This agreement and each of its provisions shall be binding upon and shall inure to the benefit of the parties hereto and their respective heirs, executors, administrators, successors, and assigns. Notwithstanding the foregoing, this agreement is personal to the Investigator and shall be assignable by the Investigator only with the written consent of Sponsor, which consent may be withheld in Sponsor's sole and absolute discretion.

9. Law Governing. This Agreement shall be governed by and construed and enforced in accordance with the laws of the State of California, without regard for its conflict of laws rules. The parties hereby submit to the exclusive jurisdiction of the courts of the State of California, in and for the County of Los Angeles, and the United States District Court for the Central District of California for the purpose of construing and enforcing this Agreement.

10. Damages. Mentor shall not be responsible for any damages, whether direct, indirect, consequential, special, punitive, or exemplary, whether foreseeable or unforeseeable, or any lost profits, incurred by the Investigator except for the payments contemplated by Article 4 of this Agreement.

11. Indemnification. Sponsor will have no liability for loss or damage and no duty to defend or hold harmless from any demands, claims, or costs of judgment resulting from:

- a) Investigator's failure to adhere to the terms of the protocol or Sponsor's written instruction concerning the use of the Trial device.
- b) Investigator's failure to comply with applicable FDA or other government requirements.
- c) Investigator's negligence or willful misconduct by the investigator, his agents or employees.

12. Insurance. Investigator shall maintain a policy or program of insurance at levels sufficient to cover any losses to Mentor and Trial participants.

13. Severability of Provisions. In the event any one or more of the provisions of this Agreement shall for any reason be held to be invalid, illegal, or unenforceable in any respect, such invalidity, illegality, or unenforceability shall not affect any other provision hereof, and this Agreement shall be construed as if such invalid, illegal, or unenforceable provision had never been contained herein.

14. Integration. This Agreement constitutes the entire understanding and agreement between the parties with respect to the transactions contemplated herein and supersedes all previous communications, representations, or understandings, either oral or written, between the parties relating to the subject matter hereof, all of which are merged herein.

15. Agreement Controls. This Agreement shall control whenever the provisions of any subordinated document conflict with this Agreement.

16. Termination. Sponsor may terminate the Trial and this Agreement at any time on ten days written notice to Investigator. Sponsor shall not be liable to Investigator for any costs or damages suffered due to such termination.

17. Publication. Sponsor acknowledges that the Investigator and his/her collaborators shall be free to publish the background, methods and results of their own research without restraint. Prior review of any proposed manuscript or abstract will be provided to Sponsor to prevent premature disclosure of trade secrets or proprietary information. This review will be done by the Investigator submitting to Sponsor a copy of any manuscript or abstract and submitted for consideration for publication or to a conference, as applicable, no later than 30 days before such manuscript or abstract is so submitted. The Investigator acknowledges that the Sponsor reserves the right to publish and present the overall study results, including assigning authorship. Sponsor acknowledges that all active Investigators will be recognized for their contributions with any manuscript or presentation.

18. Signatures.

Investigator Signature

Date

Director, Clinical Programs, Mentor Corporation

Date

Attachment A

Compensation Addendum for Investigator for the Core Gel Study

Sponsor: Mentor Corporation, 201 Mentor Drive, Santa Barbara, CA 93111

Investigator:

This appends the Investigator Agreement for the Core Gel Study. Mentor Corporation (Sponsor) and _____, M.D. (Investigator), agree to the following:

1. The Sponsor shall compensate for anticipated enrollment and follow up for the study population. A patient shall be considered qualified if she is enrolled according to the inclusion/exclusion criteria, has signed an informed consent prior to surgery, is treated according to the study protocol, and the Sponsor receives all enrollment paperwork.
2. The Sponsor will pay the investigator \$_____/patient in compensation, according to the following payment schedule. Payment will be made monthly, based on Mentor receiving forms that are ready for entry into a database. Investigators will not be paid for incomplete or inaccurate forms.

Timeframe	Compensation	Timeframe	Compensation
Baseline		5 years	
6 months		6 years	
1 year		7 years	
2 years		8 years	
3 years		9 years	
4 years		10 years	

3. The Sponsor agrees to compensate as necessary for the expenses incurred by trial sites. These expenses require pre-approval by Mentor.

Investigator Signature

Date

For tax purposes, please print the name of the individual/organization as it is to appear on compensation check. Also provide the Social Security Number (SSN) or Tax ID#:

Investigator/Organization Name (printed)

SSN/Tax ID#

Attachment B

Compensation Addendum for Study Coordinator for the Core Gel Study

Sponsor: Mentor Corporation, 201 Mentor Drive, Santa Barbara, CA 93111

Study Coordinator:

This appends the Investigator Agreement for the Core Gel Study. Mentor Corporation (Sponsor) and Amy Fenstermacher (Study Coordinator), agree to the following:

1. The Sponsor shall compensate for anticipated enrollment and follow up for the study population. A patient shall be considered qualified if she is enrolled according to the inclusion/exclusion criteria, has signed an informed consent prior to surgery, is treated according to the study protocol, and the Sponsor receives all enrollment paperwork.
4. The Sponsor will pay the study coordinator \$█/patient in compensation, according to the following payment schedule. Payment will be made monthly, based on Mentor receiving forms that are ready for entry into a database. Investigators will not be paid for incomplete or inaccurate forms.

Timeframe	Compensation	Timeframe	Compensation
Baseline	█	5 years	█
6 months	█	6 years	█
1 year	█	7 years	█
2 years	█	8 years	█
3 years	█	9 years	█
4 years	█	10 years	█

Study Coordinator Signature

Date

For tax purposes, please print the name of the Study Coordinator/organization as it is to appear on compensation check. Also provide the Social Security Number (SSN) or Tax ID#:

Study Coordinator/Organization Name (printed)

SSN/Tax ID#