SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name:	Silicone Gel-Filled Breast Implants
Device Trade Name:	MemoryShape™ Breast Implants
Device Procode:	FTR
Applicant's Name and Address:	Mentor Worldwide LLC 201 Mentor Drive Santa Barbara, California 93111
Date(s) of Panel Recommendation:	None
Premarket Approval Application (PMA) Number:	P060028
Date of FDA Notice of Approval:	June 14, 2013
Expedited:	Not Applicable

II. INDICATIONS FOR USE

The MemoryShape™ Breast Implants are indicated for females for the following uses (procedures):

- Breast augmentation for women at least 22 years old. Breast augmentation includes primary breast augmentation to increase the breast size, as well as revision surgery to correct or improve the results of a primary breast augmentation surgery.

- Breast reconstruction. Breast reconstruction includes primary reconstruction to replace breast tissue that has been removed due to cancer or trauma or that has failed to develop properly due to a severe breast abnormality. Breast reconstruction also includes revision surgery to correct or improve the result of a primary breast reconstruction surgery.

III. CONTRAINDICATIONS

Breast implant surgery should not be performed in women:

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

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the MemoryShape™ Breast Implant labeling.

V. DEVICE DESCRIPTION

Each MemoryShape™ Breast Implant is composed of a textured silicone elastomer shell and is filled with silicone gel. The implants are single lumen with a patch on the posterior side. They are available in a contour profile (shaped) design in varying sizes. There are raised orientation marks on the anterior and posterior of the implant. The implants are provided dry-heat sterilized with a 5-year shelf life from the date of sterilization. Figure 1 shows a diagram of the implant and Figure 2 shows the orientation marks.

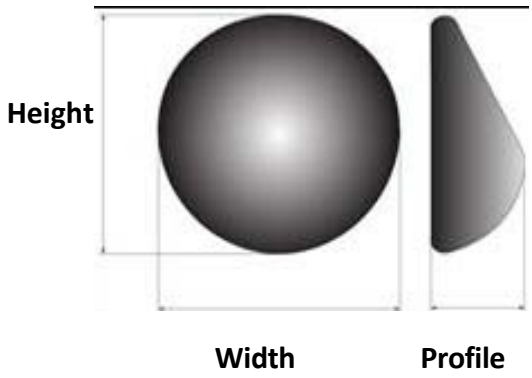

Figure 1: Mentor MemoryShape™ Breast Implant

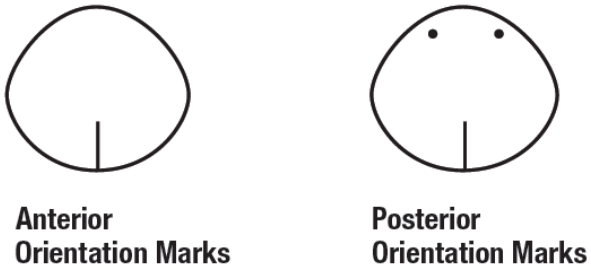

Figure 2: Orientation Marks

Table 1 shows the MemoryShape™ Breast Implant styles. Table 2 shows the general device material for the shell, patch, and gel components.

Catalog Number	Style	Volume (cc)	Width (cm)	Height (cm)	Projection (cm)	Number of Sizes
354-0908/1708	Style MM or 321: Medium Height, Moderate Profile	120-775	9.0-17.0	8.5-16.0	3.3-5.9	15

Table 1: MemoryShape™ Breast Implant Style

Component	Raw Material
Shell, Inner/Outer Layers	High Consistency, High Tear Strength Silicone Elastomer
Shell, Barrier Layer	Diphenyl Silicone Elastomer
Shell, Textured Layer	High Consistency, High Tear Strength Silicone Elastomer
Patch Assembly	High Consistency, High Tear Strength Silicone Elastomer Diphenyl Silicone Elastomer
Gel	High Purity Silicone Gel
Position Indicator	High Consistency, High Tear Strength Silicone Elastomer

Table 2: MemoryShape™ Device Materials

The principal features distinguishing this style from Mentor's previously approved MemoryGel® Silicone Gel-Filled Breast Implants (P030053) are the:

- More cohesive gel fill
- Device shape [Figure 1]
- Ranges of sizes [Table 1]
- Presence of orientation marks [Figure 2]

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several other alternatives for the augmentation or reconstruction of the breast with silicone gel breast implants. Alternative procedures include saline-filled breast implant surgery, external prostheses, autogenous tissue grafts (e.g., fat grafting), tissue-flap surgeries (e.g., transverse rectus abdominus muscle, latissimus dorsi muscle, gluteal muscle), or no treatment. Each alternative has its own advantages and disadvantages. A patient should fully discuss these alternatives with her physician to select the method that best meets expectations and lifestyle.

VII. MARKETING HISTORY

Mentor MemoryShape™ Breast Implants, formerly known as Mentor Contour Profile Gel (CPG) Breast Implants, were introduced in more than 35 countries worldwide between 2000 and 2002, and are still supplied to these markets. The Mentor MemoryShape™ Breast Implants have not been withdrawn from any foreign market for any reason relating to the safety and effectiveness of the device.

In February 2002, Mentor received FDA approval for the MemoryShape™ Core Study, a 10-year study to assess safety and effectiveness in augmentation, reconstruction, and revision patients.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Below is a list of the potential adverse effects (e.g., complications) associated with the use of the device.

- Reoperation (additional surgeries)
- Implant removal with or without replacement
- Implant rupture
- Capsular Contracture
- Wrinkling
- Asymmetry
- Implant displacement
- Implant palpability/visibility
- Scarring
- Ptosis
- Breast Pain
- Changes in nipple and/or breast sensation

- Infection (including Toxic Shock Syndrome)
- Hematoma
- Seroma
- Breastfeeding difficulties
- Calcium deposits
- Extrusion
- Necrosis
- Delayed wound healing
- Breast tissue atrophy/chest wall deformity
- Lymphadenopathy
- Bruising
- Calcification
- Metastatic disease
- Erythema
- Excess skin/tissue
- Fibrocystic disease
- Granuloma
- Hypertrophic scarring
- Intermittent Pop
- Irritation/Inflammation
- Itching
- Lack Of Projection
- Loss Of Definition Of Inframammary Fold
- Mass/cyst
- Miscarriage
- Muscle Atrophy
- Nipple complication
- Paresthesia
- Rash
- Skin Lesion
- Swelling
- Symmastia
- Tenderness/ Soreness
- Wound Dehiscence
- Gel fracture
- Connective tissue disease (CTD)
- CTD signs and symptoms
- Neurological disease
- Neurological signs and symptoms

- Cancer
- Lymphoma
- Suicide
- Potential effects of offspring

For the specific adverse events that occurred in the clinical studies, please see Section X below.

IX. SUMMARY OF PRECLINICAL STUDIES

The preclinical studies are divided into five sections – chemistry, toxicology, mechanical, modes and causes of device failure, and shelf life.

A. Chemistry Data

Chemical testing was performed on the major components (shell and gel) of Mentor's product. The chemical data support the biological safety of this device for its intended use because the values for concentrations of low molecular silicones and heavy metals are well below known toxicity levels.

1. Equilibrium Swell Ration, Sol Fraction and Crosslink Density

The equilibrium swell ratio, sol fraction, and crosslink density of MemoryShape™ Breast Implants for gel and shells were measured. Gel and shell samples that had been given an additional thermal post cure treatment were also subjected to the same analysis to demonstrate that the gel and shells were fully cured during standard processing. The results are presented in the table below.

The shell and gel results were not significantly different after the additional thermal cure treatment ($p \geq 0.05$), and support the conclusion that the gel filler and shells exhibited complete cure after normal processing.

	Network Chain Molecular Weight (g/mol)	Molar Crosslink Density (mol/cm^3)	Crosslink Chain Density ($chain/cm^3$)	Swell Ratio	Extractables (%)	Recovery (%)
Finished Device Gel, Sample M:V ~ 1:100						
Average	5.53E+05	1.77E-06	1.07E+18	32.9	79.7	94.26

	Network Chain Molecular Weight (g/mol)	Molar Crosslink Density (mol/cm^3)	Crosslink Chain Density (chain/cm^3)	Swell Ratio	Extractables (%)	Recovery (%)
Standard Deviation (SD)	2.26E04	7.18E-08	4.32E+16	0.7	1.2	1.23
SD/Average	0.04	0.04	0.04	0.02	0.02	0.01
Finished Device Shell, Sample M:V ~ 1:200						
Average	8.57E+03	1.30E-04	7.85E+19	4.0	9.4	101.13
Standard Deviation	1.32E+03	2.02E-05	1.22E+19	0.1	0.5	1.48
SD/Average	0.15	0.16	0.16	0.03	0.05	0.05

Table 3: Crosslink Density, Swell and Extractables of Gel and Shell from MemoryShape™ Breast Implants

2. Volatile Extractables

The volatile profiles of MemoryShape™ Breast Implants, shell and gel filler were analyzed and the results are provided in the table below. The total volatile content of the device was approximately 18 parts per million (ppm). The levels of volatile cyclic dimethylsiloxanes (D3-D5) were below 10 ppm. Other volatile constituents were linear dimethylsiloxanes (MM-MD2M) and solvents or solvent impurities, all were present in trace quantities. The volatile extractable testing results are comparable to results seen in previously approved breast implant devices.

Compound	Shell Not Exposed to Gel (µg/g)	Gel Filler (µg/g)	Shell (µg/g)	Whole Device (µg/g)
Cyclic Dimethyl Siloxanes				
D_3[1]	0.14	1.30	1.73	1.34
D_4[1]	0.05	4.08	2.61	3.95
D_5[1]	0.33	9.47	5.34	9.11
Linear Dimethyl Siloxanes				
Methoxytrimethylsilane[2]	3.02	ND	7.67	0.66
Dimethoxydimethylsilane[2]	0.10	ND	0.40	0.03
Methyltriethoxysilane[2]	0.10	ND	0.40	0.03
Tetramethyldiethyldisiloxane[2]	ND	ND	ND	ND
Miscellaneous Solvent Residues and Others				
Acetone[2]	0.94	ND	2.57	0.22
Isopropanol[1*]	4.58	ND	20.91	1.80

Compound	Shell Not Exposed to Gel (µg/g)	Gel Filler (µg/g)	Shell (µg/g)	Whole Device (µg/g)
2-Pentanone[2]	ND	ND	NA	NA
Methyl Butanoate[2]	NA	ND	NA	NZ
4-Methyl-3-pentne-2-one[2]	ND	ND	ND	ND
Ethylbenzene[1*]	0.05	NA	0.07	0.01
m-&p-Xylenes[1]	0.18	0.32	0.31	0.32
o-Xylene[1]	0.07	0.13	0.11	0.13
alpha-Pinene[2]	ND	ND	ND	ND
Cyclohexanone[1]	ND	0.21	<0.14	0.20
1-Ethyl-2-methylbenzene[2]	ND	ND	ND	ND
Decane[1]	ND	ND	ND	ND
Benzaldehyde[2]	0.04	ND	0.04	0.00
Trimethylbenzene[2]	ND	0.05	0.08	0.05
Limonene[2]	0.06	ND	NA	NA
Undecane[1]	ND	ND	ND	ND
Acetophenone[2]	NA	ND	0.04	0.00
Dodecane[1]	ND	ND	ND	ND
Total Volatiles (µg/g device)	**9.66**	**15.56**	**<42.42**	**17.85**

ND = Not Detected, S/N <3.0
NA = Not Applicable. At least one of the replicates has a ND value. Data preceded with a "<" symbol meaning a less than method detection limit value.
[*] Integration based on Extracted Ion Chromatogram.
[1] Measurement based on external and internal standard calibrations.
[2] Measurement based on the response factor of closest internal standard.

Table 4: Volatile Profiles of MemoryShape™ Breast Implants, Shell and Gel Filler

3. Total Extractables

Total extractables were determined through gravimetric measurements on MemoryShape™ Breast Implants, shells and gel. Device extracts were obtained via Soxhlet methylene chloride extractions. It should be noted that exposure to methylene chloride produces dramatic swelling of the gel, facilitating the release of silicone fluid entangled within the interpenetrating gel network. The extractions were conducted separately on device components (gel filler and shell assembly).

The mean gravimetric determination of total extractables showed shells not exposed to gel (unfilled) yielded 1.7%, shell assemblies from finished product yielded 10.3%, and gel filler yielded 77.1%. Whole devices yielded 71.5% total extractables by combining

the weight averaged values of the shell and gel extractables. Results are listed in table 5. The results of the total extractables testing are comparable to results seen in previously approved breast implant devices.

Device Component	MemoryShape™ Device % Extractable	MemoryShape™ Shell Not Exposed to Gel (unfilled) % Extractable
Shell Assembly	10.26	1.70
Gel Filler	77.1	NA
Whole Device	71.5	NA

%Total extractable in whole devices = sum (%extractable found in individual component x component wt)/whole device wt

NA = not applicable

Table 5: Total Extractable Using Gravimetric Measurement

4. Semivolatile Extractables

A gas chromatography/mass spectrometry - direct liquid injection method was used to determine the semivolatile compounds (compounds with molecular weights between about 200 – 1500 Daltons) present in the methylene chloride extracts of the product. The target analytes included in the study were silicone raw materials and intermediates, processing aids, solvents, and/or additives used in the fabrication of the devices. Samples analyzed consisted of finished MemoryShape™ Breast Implants, shell and gel.

Whole devices yielded 71.5% total extractables. The semivolatile compounds identified were primarily cyclic (D3-D21) and linear dimethylsiloxanes (MD8M- MD17M), with minor concentration levels of monovinylcyclosiloxanes (VD13- VD20) and a trace amount of dimethyldiphenylsiloxane (D3P2). There were also small quantities of some unidentified siloxane compounds. Monovinylsiloxanes and linear dimethylsiloxanes were present in the gel and shell of finished product but were absent in nongelled shells. The monovinylsiloxanes and linear dimethylsiloxanes in device shells are presumably attributed to components in the gel. Quantities of monovinylsiloxanes and linear dimethylsiloxanes in both gel and shell of finished devices were similar. Results are listed in table 6. The results of the semivolatile extractables testing are comparable to results seen in previously approved breast implant devices.

(Gel – 3 devices from 1 lot; shells – 3 devices from 1 lot)

	Shell Not Exposed to Gel	Gel Filler	Shell	Whole Device
Compound	**µg/g or ppm**			
Cyclic Dimethyl Siloxanes				
D_3[1]	ND	1.68	ND	1.53
D_4[1]	ND	3.11	2.49	3.06
D_5[1]	ND	9.96	5.93	9.62
D_6[1]	ND	10.12	8.61	9.99
D_7[2]	NA	11.81	8.07	11.49
D_8[2]	29.08	9.92	12.08	10.10
D_9[2]	58.29	9.30	11.26	9.47
D_{10}[2]	85.17	12.15	11.65	12.11
D_{11}[2]	137.43	29.46	26.92	29.24
D_{12}[2]	162.56	39.81	29.96	38.98
D_{13}[2]	178.21	66.40	36.22	63.84
D_{14}[2]	483.74	142.57	113.22	140.08
D_{15}[2]	400.81	226.35	134.97	218.60
D_{16}[2]	443.43	306.08	163.49	293.99
D_{17}[2]	479.38	687.50	300.80	654.72
D_{18}[2]	352.01	709.83	299.21	675.02
D_{19}[2]	280.59	633.74	297.25	605.22
D_{20}[2]	343.90	824.40	434.57	791.36
D_{21}[2]	<298.34	1209.17	483.00	1147.61
Linear Dimethyl Siloxanes				
MD_8M[1]	NA	<3.50	ND	3.20
MD_9M[1]	ND	7.86	NA	7.20
$MD_{10}M$[1]	ND	15.58	<17.63	15.75
$MD_{11}M$[2]	ND	25.58	<17.63	24.91
$MD_{12}M$[1]	ND	57.59	32.25	55.45
$MD_{13}M$[2]	ND	89.51	47.18	85.93
$MD_{14}M$[2]	ND	117.93	60.84	113.09
$MD_{15}M$[2]	ND	142.88	65.11	136.28
$MD_{16}M$[3]	ND	148.99	60.27	141.47
$MD_{17}M$[2]	ND	162.81	52.47	153.46
Vinyl-modified Cyclic Dimethylsiloxane				
$D^{Vi}D_{13}$[2,4]	ND	3.01	ND	2.76
$D^{Vi}D_{14}$[2,4]	ND	13.94	NA	12.76
$D^{Vi}D_{15}$[2,4]	ND	20.37	30.68	21.25
$D^{Vi}D_{16}$[2,4]	ND	29.76	33.62	30.09
$D^{Vi}D_{17}$[2,4]	ND	26.06	<48.35	27.95
$D^{Vi}D_{18}$[2,4]	ND	36.15	<43.11	36.74
$D^{Vi}D_{19}$[2,4]	ND	26.47	46.14	28.14
$D^{Vi}D_{20}$[2,4]	ND	157.24	ND	143.91
$D^{Vi}D_{21}$[2,4]	ND	ND	ND	ND

	Shell Not Exposed to Gel	Gel Filler	Shell	Whole Device
Compound	**µg/g or ppm**			
Phenyl-modified Cyclic Dimethylsiloxanes				
$D_4D^{Ph\,2}$	<18.88	ND	ND	ND
$D_5D^{Ph\,2}$	<18.88	ND	ND	ND
$D_6D^{Ph\,2}$	<18.88	ND	ND	ND
$D_7D^{Ph\,2}$	23.00	ND	ND	ND
$D_3D^{Ph}{}_2(1)^2$	40.40	ND	<15.45	1.31
$D_3D^{Ph}{}_2(2)^2$	35.73	ND	NA	NA
$D_4D^{Ph}{}_2(1)^2$	<18.88	ND	ND	ND
$D_4D^{Ph}{}_2(2)^2$	<18.88	ND	ND	ND
$D_4D^{Ph}{}_2(3)^2$	<18.88	ND	ND	ND
Miscellaneous Siloxanes				
Siloxane[3]	ND	21.48	ND	19.66
Solvent Residues and Plasticizers				
o-Xylene[1]	ND	ND	ND	ND
Di(Ethylhexyl) Phthalate[1]	ND	ND	ND	ND
Total Semivolatiles (µ g/g)	**<3945.35**	**<6050.07**	**<2950.43**	**<5786.94**

ND = Not Detected, S/N < 3.0.
NA = Not Applicable. At least one of the replicates has a ND value.
Data preceded with a "<" symbol meaning a less than method detection limit value.
[1] Measurement based on external and internal standard calibrations
[2] Due to unavailability of external standards, measurement is estimated, based on calibrated response factors of closest homologue.
[3] Measurement based on the response factor of closest internal standard.
[4] Tentative identification based on MS pattern.

Table 6: Semivolatile Analysis

5. Heavy Metal Analysis

The analysis for total heavy metals content was conducted on MemoryShape™ Breast Implants, gel and shell. The analysis employed a microwave-assisted mixed solution of aqua regia and hydrofluoric acid (in 5:1 ratio) digestion procedure for complete decomposition of the silicone matrix and the total solubilization of the analytes. The subsequent identification and quantification of the metal species were accomplished by inductive coupled plasma/mass spectrometry (ICP/MS).

The results indicated there were 5.3 and 8.0 ppm of platinum present in the gel filler and shell assembly of MemoryShape™ Breast Implants respectively. Several other metals

were measured at trace levels in MemoryShape™ Breast Implant gel and and/or shell. The total heavy metal results demonstrate that for MemoryShape™ Breast Implants platinum was the only metal present in significant quantities. The results of the heavy metal analysis testing are comparable to results seen in previously approved breast implant devices.

Platinum is a metal used as a catalyst in the manufacture of the shell and gel materials of silicone breast implants. The small amounts of platinum remaining in the product may enter the body, either by diffusing through the intact shell (i.e., through gel bleed) or through an implant rupture. Based on a review of the published literature and other available data, FDA has concluded that the platinum contained in breast implants is in the zero oxidation state, which has the lowest toxicity, and thus, does not pose a significant risk to women with silicone breast implants. The breast implants under this PMA specifically, were not tested for zero oxidation state.

FDA has posted a Backgrounder on its website that provides a brief summary of the key scientific studies on platinum and silicone gel-filled breast implants: http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/ImplantsandProsthetics/BreastImplants/UCM064040

Metal	Method Detection Limit[1]	Gel	Shell	Total Amount in Device[2]
Antimony	0.0007	0.0121	0.0216	0.0129
Arsenic	0.1520	ND	ND	<0.1520
Barium	0.0013	ND	0.0112	0.0022
Beryllium	0.0005	ND	ND	<0.0005
Cadmium	0.0005	ND	0.0011	0.0006
Chromium	0.0052	0.0649	0.0776	0.0660
Cobalt	0.0005	ND	ND	<0.0005
Copper	0.0006	0.0455	0.1282	0.0526
Lead	0.0003	0.0023	0.0027	0.0023
Mercury	0.0012	0.0055	ND	0.0051
Molybdenum	0.0015	0.0030	0.0015	0.0029
Nickel	0.0048	ND	ND	<0.0048
Platinum	0.0015	5.3355	8.0339	5.5690
Selenium	0.0266	0.0501	0.0905	0.0536
Silver	0.0005	ND	ND	<0.0005
Tin	0.0019	0.0356	0.1047	0.0416
Titanium	0.0032	0.2296	0.2022	0.2273
Vanadium	0.0170	0.0179	ND	0.0178

Metal	Method Detection Limit[1]	Gel	Shell	Total Amount in Device[2]
Zinc	0.0218	ND	0.4233	0.0564

Data preceded with a "<" symbol meaning a less than method detection limit value.
[1]Highest value of all analysis sequences for the study
[2]Total amount in device = [(conc. in gel * weight of gel) + (conc. in shell * weight of shell)]/device weight = [(conc.in gel * 302.9g) + (conc.in shell * 28.5579g)]/331.4g

Table 7: Heavy Metal Analysis Testing

6. Silica Filler

X-ray diffraction studies on the elastomer shell confirm that the silica used as reinforcing filler material is in the amorphous form, not in crystalline form.

B. Toxicology Data

Mentor provided both pharmacokinetic and biocompatibility testing to address the biological safety of this device.

Pharmacokinetics

Mentor cited a number of experiments in its PMA in which ^{14}C-labeled polydimethylsiloxanes were injected subcutaneously in animals. Most of the radioactivity (94-99.97%) remained at the injection sites. In one experiment, less than 0.02% was found to have migrated to different tissues. Raposo do Amaral, et al.[i] injected rats with 2ml of silicone gel at two different sites and followed the animals for various time periods up to 450 days. Silicone was not detected in the heart, spleen, liver, stomach, or gonads, but it could be detected locally surrounding the tissue capsules at the implantation sites. No silicone was found in the regional lymph nodes.

Swanson, et al.[ii] evaluated 3 dogs 10 years after implantation with silicone elastomer joint implants. At the postmortem examinations, there was little evidence of migration. Particles were found around the joints, but no particles were found at distant sites except for a few particles in the axillary lymph nodes. Swanson also reported on the autopsy of a rheumatoid arthritis patient who had silicone implants in hands, radial heads, and feet beginning 12 years before death. Silicone particles were found in giant cells in the synovium with minimal inflammatory cells, but no focal necrosis. Some silicone was also found in giant cells in an axillary node.

With regard to the migration of low molecular weight mixtures of cyclic siloxanes (e.g., D4, D5, D6), Kala, et al.[iii] injected a distillate of cyclic siloxanes in the suprascapular area in mice. At 1 month, the highest cyclosiloxane levels were detected in the mesenteric lymph nodes, ovaries, and uterus, but all organs contained some cyclosiloxanes.

The distribution pattern changed over the course of a year. The high dose used far exceeded the level of low molecular weight siloxanes present in Mentor's MemoryShape™ Breast Implants. The survival of the mice for one year at these levels of cyclosiloxane exposure indicates a high level of safety.

Plotzke et al.[iv] published a pharmacokinetic study of ^{14}C-labeled D4 in Fischer 344 rats following single and multiple inhalation exposures to 7, 70, or 700 ppm D4. Based on these data, a physiologically-based pharmacokinetic (PB/PK) model was developed for D4 by Andersen et al.[v,vi] It was concluded that "high pulmonary and hepatic clearance, coupled with induction of metabolizing enzymes at high exposure concentrations, rapidly remove free D4 from the body and ensure that there is no accumulation on multiple exposures."

Biocompatibility Testing

The biocompatibility testing listed below was conducted on the major device components (shell, gel and patch), and/or finished sterilized devices, as described in ISO 10993. This testing demonstrated the biocompatibility of the MemoryShape™ Breast Implants.

1. Cytotoxicity (ISO Elution Method)
2. ISO Intracutaneous Study (Rabbit)
3. USP and ISO Systemic Toxicity (Mouse)
4. USP Pyrogenicity (Material Mediated)
5. ISO Subcutaneous Implantation (20 cc miniature device, 12 weeks in rabbits, with histopathology)
6. ISO Sensitization (Maximization Method)
7. Genotoxicity
    a. Bacterial Reverse Mutation Assay - saline and ethanol extracts
    b. Unscheduled DNA Synthesis Assay in Mammalian Cells In Vitro - saline and ethanol extracts
    c. Chromosome Aberrations in Chinese Hamster Ovary (CHO) Cells - saline and ethanol extracts
    d. Mouse Lymphoma Assay – saline and ethanol extracts
    e. Mouse Micronucleus Assay - saline and corn oil extracts
8. Immunotoxicity

9. Autoantibody Production
10. Adjuvancy
11. Reproduction and Developmental Studies
    a. Reproduction/Teratology (shell)
    b. Extended One-Generation Reproductive and Developmental Study (gel)
    c. Reproductive and Developmental Toxicity Studies - Dow Corning (gel)
12. Chronic Toxicity/Carcinogenicity

Based on common materials and manufacturing processes, testing conducted on Mentor's Round MemoryGel® Silicone Gel-Filled Breast Implants (P030053) was considered directly relevant and applicable to MemoryShape™ Breast Implants. The table below summarizes the tests performed on each device, and the device/device components:

Device/Component Tested	Biological Tests Performed*
MemoryShape™ Breast Implant (P060028) (sterile device)	1, 2, 3, 4, 5, 6
MemoryGel® Breast Implant (P030053):	
- Sterile Device[1]	- 1, 2, 3, 4, 5, 7
- Textured Shell Only[2]	- 8, 10 3, 11a, 12
- Smooth Shell Only[2]	- 8, 9, 11a, 12
MemoryGel® Breast Implant Gel Only (P030053)	8[4], 10[4], 11b[5], 11c[4], 12[4]

* Numbers correspond to numbered tests listed above
[1] Made with SiTech gel and SiTech shell dispersions
[2] Made with Polymer Technology Corp. shell dispersions (an equivalent material from a former vendor)
[3] MED 4750 textured layer on room temperature vulcanized (RTV) shell
[4] Dow Corning Q7-2167/Q7-2168 gel (an equivalent material from a former vendor)
[5] SiTech Gel-2167 Gel-2168

Table 8: Biocompatibility Testing Conducted

The biocompatibility testing is summarized below (note that numbers below do not correspond to numbers in table 8 above).

1. Cytotoxicity

Cytotoxicity testing was performed on the elastomer, thermoforms (packaging material), the implant container lid, the propylene mold release, device-contact imprinting foam, and total 100ml gel prosthesis using mouse fibroblast L929 cells. The cells were observed for lysis and changes in cell morphology or cell death. For the acceptance criteria, the negative control must have been a grade of 0 (reactivity none), the positive control must have produced a zone of lysis (reactivity moderate, to severe), and the three monolayers exposed

to the test article showed no greater than a grade of 2 (reactivity mild). The results showed that the test articles were non-cytotoxic.

2. Short Term Irritation and Implantation

The textured shell material, a thermoform, imprinting foam, mandrel materials, and laser-marked patches were tested for irritation. Each was extracted into saline and cottonseed oil (CSO) and injected subcutaneously in rabbits. The injection sites were observed for edema and erythema. For the acceptance criterion, the mean macroscopic scores for test implants were compared to mean scores of the control sites. The requirements of the test were met if the difference between test and control score means (macroscopic) was not greater than 1.0. There was no significant reaction to any of these materials.

The imprinting foam device contact material evaluated by the same tests did not produce significant irritation.

The testing for some device components was adjusted to reflect their use. The mold release material (a processing aid) was sprayed onto the MED 4750 elastomer, dried, and extracted into saline and CSO and tested. Strips of elastomer (1mm x 10mm) with dried mold release material were implanted intracutaneously through a 16 gauge needle in rabbits. The controls were USP strips. The implants remained for 4 and 12 weeks, and the sites were examined grossly and histologically. The mold release was scored as a slight irritant based on a microscopic evaluation of capsule size and the tissue reaction.

A dermal irritation test was performed on the same materials. For this test, the sample was placed onto abraded skin and covered with tape. The wounds were observed 24 hours later and again at 72 hours after application. The scoring is for erythema and edema. No significant irritation was observed.

A 100ml textured gel implant was tested using 60cm^2 per 20ml of saline or CSO for extraction. Extracts of the complete implants showed no significant irritation (erythema or edema).

Groups of one of the laser-marked patches in the CSO (cottonseed oil) group showed moderate irritation. Because the reactivity to the CSO extracts is usually higher than the reaction to the saline extracts, this may have added to the effect. FDA concluded during its review of P030053 that none of the device components causes significant irritation.

3. Acute Systemic Toxicity

Extracts for testing were prepared by using 60cm^2 per 20ml of solvent of each device components for extraction into saline and cottonseed oil. The saline extracts were injected

into mice intravenously at 50 ml/kg, and the oil extracts were injected intraperitoneally at the same dose. The device components tested include the MED4750 shell, a polycarbonate thermoform, the propylene mold release, the polyurethane foam, a textured gel-filled prosthesis, a SiTech smooth prosthesis, and laser-marked patches. The animals were observed for toxic signs. If during the observation period, none of the mice treated with the individual test extract exhibited a significantly greater reaction than the corresponding control mice, the test extract met the test requirements. No toxicity was observed.

The Ertalyte (a polyethylene terephthalate-based plastic) mandrels were extracted at the same ratios, 60cm^2 but into 5% alcohol in saline, polyethylene glycol (PEG), and cottonseed oil at 121°C for 1 hour. The PEG and CSO extracts were injected intraperitoneally. No significant toxicity was observed in this test.

4. Hemocompatibility

Hemocompatibility testing was conducted by measuring the extent of red cell lysis produced by extracts of device components. Suspensions of rabbit red cells were freshly prepared. A sample of rabbit red cells were added to each of the following tubes: a negative control tube with 10ml of saline, a positive control with 10ml of water, and 2g of test materials extracted in 10ml of saline. The tubes were incubated at 37°C for 1 hour, centrifuged, and the absorbance at 545nm was measured. The percent hemolysis is the absorbance of the sample times 100 divided by the absorbance of the positive control. The mold release material was tested after being sprayed onto 30cm^2 and 90cm^2 sections of elastomer and extracted. Both smooth and textured devices elastomers were evaluated. For the acceptance criteria, an average hemolytic index of the triplicate test samples was compared to the negative control. A hemolytic index of 2% or less was considered to be nonhemolytic. No significant hemolysis was seen in any of these extracts.

5. Pyrogenecity

Rabbit pyrogen studies on a SiTech textured gel-filled prosthesis were conducted by measuring rabbit temperature increases following intravenous administration of device extracts in New Zealand White Rabbits. The test article was a complete 100ml textured prosthesis extracted into 60cm^2 per 20ml of sterile non-pyrogenic saline. The acceptance criterion was that no single animal showed an increase of 0.5ºC or more above its baseline temperature. The rabbit temperature rise was within acceptable limits. The test materials were, therefore, considered non-pyrogenic. The SiTech smooth gel- filled prosthesis was tested in the same way. The results showed that the test articles were non-pyrogenic.

6. Immunotoxicity

There were three groups of immunotoxicity tests conducted by implanting the test materials subcutaneously in B6C3F1 mice. Three shell doses were used, 14mm^2, 28mm^2, and 57mm^2. The patch was tested only at 28mm^2. Cyclophosphamide was the positive control at 25mg/kg injected intraperitoneally. For the acceptance criteria, the animals were regularly observed for any toxic signs.

In the first test, the low bleed shell was tested. The parameters evaluated were body weights, spleen and thymus weights, hematology, including RBCs, hemoglobin, hematocrit, MCV, MCH, and MCHC, a differential count of leukocytes. In the spleen, IgM antibody forming cells to sheep erythrocytes, splenic T cells, $CD4^+$, $CD8^+$, and B cells were all enumerated. For total T-cell enumeration, a Thy 1.2^+ monoclonal antibody was used. All of the observations were normal except for an increase in T cells in the spleen, as determined by the Thy 1.2^+ marker and a decrease in spleen weights in the animals exposed to the low bleed shell and patch.

An additional test was conducted to determine the cause of the increased Thy 1.2^+ responsive cells without increases in the counted T-cells. The finding was that the Thy 1.2^+ marker is non-specific and also binds to "non-immune cells." The non-immune cells were likely to have been fibroblasts that also bind the Thy 1.2^+ antibody. Thus, there were no immunological abnormalities in the first experiment.

In the second test, the smooth envelope low bleed shell was implanted in mice for ten days. There were no effects on body weight, spleen or thymus weight, or thymus histopathology. The implants did not alter the response of the spleen cell proliferation response to T-cell mitogens (Con A or Phytohemagglutinin) nor was the response to allogeneic spleen cells from DBA/2 mice altered. Taken together with the first test in the series, Mentor concluded that the smooth elastomer low bleed shell did not alter the immune response.

In the third set of experiments, the protocols are very similar to the first set of experiments. The testing was designed to test the effects of the device implantation on immune system function. None of the implants significantly affected the immune system in these mice. There were no changes in spleen weight, thymus weight, hematology (RBCs, Hb, HCT, MCV, MCH, MCHC, or leukocyte numbers or differentials). There were no differences in the ability to produce antibodies to T-dependent sheep erythrocyte antigens. There were no differences in the number of spleen cells, and no effects on the T-helper or T- suppressor populations. In conclusion, there were no significant effects of the test articles on the immunological response.

7. Sensitization

Sensitization testing was performed on MED-4750 (a textured elastomer component), the dispersion coating (400001), the mold release (400065 – after spraying on elastomer), and the laser engraved patches (104346). The Guinea Pig Maximization test was used. The CSO and saline extracts were injected intradermally, and, a week later, petrolatum with SLS was rubbed into the site. A day later, the petrolatum was removed, and test article on filter paper was applied and removed after 48 hours. Induction was tested two weeks later using a Hill Top chamber. Dermal reactions were observed 1, 2, 3, and 4 days. For the acceptance criteria, scoring grades of 1 or greater in the test group generally indicated sensitization, provided that grades of less than 1 were observed on the control animals. No significant sensitization was observed for any of the materials tested.

8. Reproductive Toxicity and Teratogenicity

A two-generation study in rats to assess the teratogenic and reproductive toxicity potential of both Mentor's Round MemoryGel® Silicone Gel-Filled Breast Implant and the Saline-Filled Breast Implant shells was conducted.

In order to exaggerate the dose of potentially extractable materials the elastomeric test material was pulverized prior to implantation, thus vastly increasing the exposed surface area. The findings of this study indicated that, compared to the controls, pulverized patched silicone elastomer mammary prosthetic shells did not cause reproductive or teratogenic effects when implanted subcutaneously in female rats in two consecutive generations. These results are consistent with published data in showing that silicone elastomer materials are neither reproductive toxicants nor teratogens in animals.

An extended one-generation reproductive and developmental toxicity study was provided in P030053 on the Mentor gel Q7-2159A. Teratogenic effects were followed in the F1 animals for systemic, developmental, neurobehavioral, and reproductive abnormalities. The animals were examined carefully for each of the examinations/tests conducted, and the qualitative findings and numerical results were provided. Gel was implanted at 0, 3, 10, and 30ml per kg. The control group was implanted with carboxymethyl cellulose. The F1 animals were examined for sex ratio, developmental markers, anogenital distance, pinna detachment, etc. Selected F1 weanlings were retained until adulthood, and examined for growth, motor activity, learning, and memory. There were no significant reproductive changes such as age of acquisition of puberty, sperm motility, etc. At necropsy, the animals were examined for anatomical teratogenic effects. There was no significant evidence of reproductive or teratogenic effects in this study. These results are consistent with published data in showing that silicone gel materials are neither reproductive toxicants nor teratogens in animals.

9. Genotoxicity

Mentor conducted genotoxicity testing using the Salmonella Reverse Mutation Assay (Ames Test), Unscheduled DNA Synthesis, the Chromosome Aberration Assay in CHO cells, and the mouse micronucleus assay. The tests were all done with and without S9 activation.

The Ames Test (Salmonella Assay) was used to test elastomer MED 4750, the dispersion coat (part 400001), the mold release, low bleed shell, and extracts of the complete 100ml implant. There were no significant genotoxic effects.

In a second set of tests, Mentor used unscheduled DNA synthesis to test the genotoxicity of Mentor's smooth round silicone gel-filled breast implants (275cc). The entire device was extracted into saline and into ethanol. The test article was extracted using 0.2g test article per ml of extraction medium. Neither extract stimulated unscheduled DNA synthesis.

In a third set of tests, Chromosome Aberration Assays were conducted in Chinese hamster ovary (CHO) Cells. Saline and alcohol extracts of a low-bleed shell gel- filled breast implant were tested. The test article was chopped into small pieces for extraction at 50°C for 72 hours with shaking. Colcemid was added 2 hours prior to harvest to inhibit cell growth. The test was performed with and without S9 activation. No increases of chromosome aberrations over the control were seen.

A fourth set of tests included an in vivo mouse micronucleus test. The test article was a 300cc Siltex® Moderate Profile Gel-filled breast implant. The device was cut into small pieces through all layers and extracted into saline and corn oil at a ratio of 1 g of device per 5 ml of extraction solvent. The positive control was cyclophosphamide, 2.5 mg/ml. The device extracts did not increase the micronucleated cells in the marrow of injected animals. There was no evidence of genotoxicity.

10. Carcinogenicity

Because of the negative mutagenicity testing and a negative mouse micronucleus test, additional carcinogenicity testing was not requested by FDA. Mentor provided several carcinogenicity tests performed using prior vendor materials as well as finished device extractable testing results that demonstrate that the materials used in Mentor's gel-filled implants are not substantially different from the materials used in the carcinogenicity studies provided.

In the first set of tests, a carcinogenicity study was conducted with albino rats using TX-1028, TX-1209, TX-1210, and TX-1211 Dow Corning gels. Each of the Dow Corning silicone gels was implanted in 50 male and 50 female rats. There were also sham operated

and no-treatment control groups. Solid state tumors were seen in all of the implantation groups. The tumors were all mesenchymal tumors, primarily fibrosarcomas. The sham operated and untreated controls did not have tumors. All other pathology was comparable across the treated groups.

In the second set of tests, a lifetime implant study was conducted with Dow Corning Q7-2159A gel in rats. This experiment utilized varying levels of test material as well as the polyethylene controls. There was no increase of non- mesenchymal tumors. The authors concluded that the silicone gel does not contain a chemical carcinogen because there was no increase of non-mesenchymal tumors across the 3 dose levels tested. That is, tumors other than solid state tumors were not increased by the device implants

C. Mechanical Data

1. Fatigue Testing

Siltex Contour Profile Gel Mammary Implants Style MM (120cc) was chosen for fatigue testing to represent Mentor's product line. All implants tested were final, sterilized versions with the minimum allowable radial shell thickness. The test set-up consisted of a uniaxial test fixture of parallel plates in a test chamber containing circulating physiologic saline solution at 37°C. The applied cyclic loads ranged from 30-100 lbs. All cyclic fatigue testing was performed at 1 Hz. A minimum of three devices were tested for all load levels. Fatigue endurance limit testing was performed at 5 Hz. Runout was established at 10 million cycles. The resulting endurance load level was 30 lbs. Based on the test set-up, all fatigue failure modes were radial tears. FDA believes that these data demonstrated that the Mentor product can withstand physiological static loading and in-vivo cyclic loading. In addition, the results are comparable to the results seen in approved breast implants.

2. Gel Bleed Testing

Mentor provided testing to identity the gel bleed constituents (including the platinum species (or other catalysts)), the rate that the gel constituents bleed out, and how that rate changes over time. Mentor's test method, which was designed to mimic in-vivo exposure to silicone gel-filled breast implants, involved the incubation of MemoryShape™ implants in porcine serum at 37°C. At specific timepoints, samples of the solution were withdrawn for analysis for low molecular weight (LMW) silicones and platinum. The results indicated that only platinum bled into the serum in measurable quantities. Platinum levels measured at 2μg by 40 days, by which time an equilibrium level was reached and no more platinum diffused through the device shell. Over 99% of the LMW silicones and platinum stayed in the implant.

With regard to the health consequences of gel bleed, the literature has reported small quantities of LMW silicone compounds, as well as platinum (in zero oxidation state), have been found to diffuse ("bleed") through an intact implant shell.[vii,viii] The evidence is mixed as to whether there are any clinical consequences associated with gel bleed. For instance, studies on implants implanted for a long duration have suggested that such bleed may be a contributing factor in the development of capsular contracture and lymphadenopathy.[ix] However, evidence against gel bleed being a significant contributing factor to capsular contracture and other local complications is provided by the fact that there are similar or lower complication rates for silicone gel-filled breast implants than for saline-filled breast implants. Saline-filled breast implants do not contain silicone gel and, therefore, gel bleed is not an issue for those products. Furthermore, toxicology testing has indicated that the silicone material used in the Mentor implants does not cause toxic reactions in test animals. It should also be noted that studies reported in the literature have demonstrated that the low concentration of platinum contained in breast implants is in the zero oxidation (most biocompatible) state.[x,xi,xii,xiii] The literature finding has been confirmed by two separate studies sponsored by Mentor. The overall body of available evidence supports that the low level of gel bleed for Mentor's product is of no clinical consequence. In addition, the results are comparable to the results seen in approved breast implants.

3. Gel Cohesion Testing

Gel cohesivity testing was performed as per ASTM F703 (cone/pendant method) using gel from final finished product. All results were below the ASTM F703 specification of <4.5cm. Gel penetration testing was performed as per a Mentor test method involving measurement of the penetration specification. All samples passed Mentor's internal penetration specifications.

D. Modes and Causes of Device Failure

1. Rupture

Mentor provided test reports and other information to characterize modes and causes of rupture of their device for a range of in vivo times, such as failure analyses of retrieved devices (i.e., retrieval study), physical property testing, assessment of manufacturing processes and surgical techniques that may impact rupture, and a review of the explant literature. The summary below is focused on retrieval data.

The MemoryShape™ explant retrieval study is designed to assess visual and physical characteristics of explanted devices, in combination with relevant clinical factors to define the mechanisms of failure for explanted devices.

The primary set of modes and causes of rupture data was a retrieval study that involved 192 explanted and returned Style MM devices from the CPG Core and Continued Access Studies. Of the 192 devices received for analysis, 4 devices were returned non-intact or ruptured. The failure mode of these 4 devices include, 1 device showing signs of sharp instrument damage and 3 devices showing a rent in the shell with no indications as to the cause. The average in-vivo time for explanted Contour Profile Gel devices was 582 days.

2. Gel Fracture

Gel fracture, or a fissure or crack, in the gel has been reported in the MemoryShape™ Implants. About 4.7% (n=9) of the 192 returned devices showed signs of gel fracture. Eight of these devices were identified during the surgical procedure and never implanted, and 1 device had been implanted for approximately 3 years.

Laboratory evaluation of the potential gel fracture of MemoryShape™ implants was conducted. Implants were subjected to various in vitro simulated mechanical stresses representing physical activity and iatrogenic events to assess the effects on the gel filler. These events included fatigue and impact, representing physical activities, mammography, and simulated surgical insertion. The physical properties of the gel were tested prior to and following exposure of devices to these events, along with photomicroscopy of the gel samples. Results from physical activity and iatrogenic event simulation showed that gel rheology is equivalent prior to and following such occurrences. No change for gel cohesivity was observed for in vitro fatigue or impact or simulated mammography or surgical insertion procedure.

The occurrence of gel fracture was low and it was noted that the rupture rate did not increase with the reported gel fractures. While there were no clinical consequences of gel fractures seen in the study, any clinical consequences of gel fracture will be investigated further in the post approval studies.

E. Magnetic Resonance Imaging (MRI) Phantom Testing

1. MRI Use for Rupture Detection

Mentor provided data showing that MRI remained a definitive tool for diagnosing the rupture or intact status of the MemoryShape™ implants.

Mentor performed a MR phantom study using MemoryShape™ and MemoryGel® Breast Implants. MR scanning was performed using a breast coil and silicone MR pulse sequence protocols. The implants were imaged at 1.5 T. In images of intact implants, the signal characteristics were found to be similar in both the MemoryShape™ and MemoryGel® devices. In images of ruptured implants, the typical manifestations ("teardrop", "keyhole",

and "linguini" characteristics) were reproduced in both sets of implant images as well. The documentation provided demonstrates that the MRI signal characteristics are similar in the MemoryShape™ and MemoryGel® implants. In addition, the documentation showed that MemoryShape™ devices can be imaged using the standard pulse sequences for silicone imaging.

2. MRI Use for Gel Fracture Detection With and Without Implant Rupture

Mentor provided testing to assess the ability of MRI to detect rupture in the presence of gel fracture and to define distinguishing characteristics of gel fracture evident via MRI.

In a phantom study, Mentor used 4 MemoryShape™ devices to test the MR image presentation when the gel has a rupture as well as a fracture. To induce shell rupture, the device was compressed between two parallel platens until shell rupture occurred. A torsional force was repeatedly placed on the implant to manually induce gel fracture. MRI was performed with a 1.5-T superconducting magnet with breast coil, used to image both implants simultaneously. Image pulse sequences performed utilized fast simulated inversion recovery (FSTIR). MR images of an intact, non-ruptured MemoryShape™ device and a fractured or ruptured device with fracture were collected simultaneously. The images were collected in two planes – cranio-caudal (CC) and mediolateral (MLO).

MR imaging demonstrated that silicone gel signal intensity was interrupted in the presence of gel fracture. In devices that were physically compressed, gel fracture appeared as a faint line, similar to air voids. In the MR imaging, the air voids caused by gel fracture, appear small, dark areas on the periphery of the shell. They are symmetric, corresponding to the load transmitted through the full projection of the device. In devices that were manually twisted to induce fracture, then immediately imaged, the line separating the gel was thicker, irregular and more hypointense on the MR image. In addition, the device shape appeared distorted. The indicative sign of device rupture is the presence of free gel on the exterior of the device. Evidence of gel fracture did not interfere with the detection of device rupture.

In summary, the study found that fractures in the gel of these devices may be detected and recognized as separation of gel to a trained reader but may not be detected or correctly interpreted by a less experienced reader, who may misinterpret these signs as indicative of rupture. Education of radiologists is therefore essential.

F. Shelf Life

Accelerated and real-time shelf life studies were performed to assure that the products perform to their specifications over time. The real-time shelf life study for MemoryShape™ Breast Implants was designed to test products at various intervals during the course of the designated shelf life. The timeframes for testing are: T=0, T=1, T=3 and T=5 years. The

real time shelf life stability testing was performed following routine sterilization, distribution simulation testing, and thermal shock cycling. All gel cohesion, shell ultimate elongation, shell tension set, shell break force, and shell/patch joint strength data passed the acceptance criteria. The MemoryShape™ Breast Implants use the same packaging configuration as Mentor's Round MemoryGel® Breast Implants. As such, the accelerated shelf life packaging data submitted in Mentor's MemoryGel® Breast Implant PMA P030053 was deemed applicable to the MemoryShape™ Breast Implants. Accordingly, the data supported a 5-year shelf life for the Mentor product.

X. SUMMARY OF MEMORYSHAPE CLINICAL CORE STUDY

Mentor performed a pivotal clinical study to establish a reasonable assurance of safety and effectiveness of MemoryShape™ Breast Implants for breast augmentation, reconstruction and/or revision in the US under IDE #G010149. Data from this clinical study were the basis for the PMA approval decision. A summary of the clinical study is presented below.

A. Study Design

Patients were treated between February 14, 2002 and September 13, 2004. The database for this PMA reflected data collected through September 30, 2010 and included 955 patients. There were 43 investigational sites.

The study is a 10-year multi-center, non-masked, open-label, clinical study to assess safety and effectiveness of 955 subjects undergoing augmentation, reconstruction, and revision (augmentation and reconstruction) procedures. Patient medical histories and baseline clinical data were collected preoperatively. Patient follow-up is at 10 weeks and then annually, starting at 1 year through 10 years. MRI scans to detect silent rupture of the implant are at 1, 2, 4, 6, 8, and 10 years. There were originally two patient cohorts – those screened for silent rupture by MRI and those who were not screened for silent rupture by MRI. On August 3, 2010, the study protocol was revised so that all subjects will be followed for symptomatic and silent rupture and will have MRI scans at years 6, 8 and 10. The results through 3 and 6 years are currently being reported, and the study remains ongoing. Mentor will periodically update labeling as more information becomes available.

1. Clinical Inclusion and Exclusion Criteria

Enrollment in the Core study was limited to patients who met the following inclusion criteria:

- Genetic female and at least 18 years old
- A candidate for:
    - Primary breast augmentation (for general breast enlargement)
    - Primary breast reconstruction (for cancer, trauma, surgical loss of breast, or congenital deformity)
    - Revision surgery (previous augmentation or reconstruction with saline-filled or silicone gel-filled implants)
- Signed the Informed Consent
- Agreed to return device to Mentor if explant was necessary
- Agreed to comply with follow-up procedures, including returning for all follow-up visits

Patients were not permitted to enroll in the Core study if they met any of the following exclusion criteria:

- Subject is pregnant
- Had nursed a child within 3 months of implant surgery
- Had been implanted with any silicone implant other than breast implants
- Had a confirmed diagnosis of any of rheumatic diseases
- Had a condition that could compromise or complicate wound healing (except reconstruction subjects)
- Subject in Augmentation cohort and had a diagnosis of active cancer of any type. (Exception is low-grade non-metastasizing skin cancer)
- Had infection or abscess anywhere in the body
- Demonstrated tissue characteristics that are clinically incompatible with implant (e.g., tissue damage resulting from radiation, inadequate tissue, or compromised vascularity)
- Possessed any condition or under treatment for any condition that, in the opinion of the investigator and/or consulting physicians(s), may constitute an unwarranted surgical risk
- Had an anatomic or physiologic abnormality that could lead to significant postoperative adverse events
- Demonstrated characteristics that are unrealistic/unreasonable with the risks involved with the surgical procedure
- Had premalignant breast disease without a subcutaneous mastectomy
- Had untreated or inappropriately treated breast malignancy, without mastectomy
- HIV positive
- Worked for Mentor or the study doctor or was directly related to anyone who worked for Mentor or the study doctor

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

2. Follow-up Schedule

All patients were scheduled to return for follow-up examinations at 10 weeks and annually through 10 years, post implantation. Breast examinations are to be conducted and information about complications are to be collected from the patients at each follow-up visit. Quality of Life (QoL) assessments occur at baseline, 1, 2, 4, 6, 8, and 10 years. A subset of patients (MRI cohort) was scheduled to have MRIs to screen for silent rupture at 1, 2, 4, 6, 8, and 10 years at the invitation of the study; as of August 3, 2010, all subjects are scheduled to undergo MRI screenings. Adverse events and complications were recorded at all visits.

The key timepoints are shown below in the table 9 summarizing safety and effectiveness.

Data Collected	Timeframe												
	Baseline	**Operative**	**10 weeks**	**1 year**	**2 year**	**3 year**	**4 year**	**5 year**	**6 year**	**7 year**	**8 year**	**9 year**	**10 year**
Subject Informed Consent	X												
Inclusion/ Exclusion Criteria	X												
Demographics/ History/ Indication	X												
Chest Measurements	X		X	X	X	X	X	X	X	X	X	X	X
Mammography (if performed)			X	X	X	X	X	X	X	X	X	X	X
Quality of Life[1]	X			X	X		X		X		X		X
Nipple/Breast Sensitivity Assessment	X		X	X	X	X	X	X	X	X	X	X	X
Rheumatic Exam	X		X	X	X		X		X		X		X
Capsular Contracture			X	X	X	X	X	X	X	X	X	X	X
Investigator Satisfaction with Implant				X	X	X							

Data Collected	Timeframe												
	Baseline	**Operative**	**10 weeks**	**1 year**	**2 year**	**3 year**	**4 year**	**5 year**	**6 year**	**7 year**	**8 year**	**9 year**	**10 year**
Surgical Information		X											
MRI Scan[2]				X	X		X		X		X		X
Adverse Events[3]		X	X	X	X	X	X	X	X	X	X	X	X

[1] Rosenberg Self Esteem Scale, SF-36, Body Esteem Scale, Breast Evaluation Questionnaire
[2] Required for randomly selected 400 subjects at study initiation. As of 8/30/10, all subjects will undergo.
[3] Including secondary procedures and re-implantations upon occurrence, whether noted at a scheduled or interim visit.

Table 9: Study Follow-Up Schedule

3. Clinical Endpoints

The assessment of safety was based on the incidence, severity, and method of resolution of all complications.

The primary effectiveness assessments of the study were the overall mean number of steps of increase in bra cup size (primary augmentation patients only) and overall mean change in chest circumference following the implantation procedure. The secondary effectiveness assessments were changes in self-reported QoL questionnaire responses and global patient satisfaction.

4. Statistical Analysis Plan

The clinical study data collected was used to produce safety and effectiveness analyses. The risk of occurrence of safety endpoints (complications, reoperations, explantations) were estimated using the Kaplan-Meier (KM) method. Reoperations and explantations were analyzed to provide a frequency distribution of the reasons for the procedures, and a frequency distribution of the various reoperation procedures was produced.

Effectiveness analyses include an assessment of changes in bra cup size (primary augmentation patients only) and circumferential chest size, patient satisfaction, and quality of life measures (Rosenberg Self Esteem Scale, Body Esteem Scale, SF-36, and the Breast Evaluation Questionnaire) from baseline to post-implantation.

The study is ongoing and results through 6 years are reported. Data will continue to be analyzed and reported to FDA at regular study intervals. In addition, Mentor

will periodically update the labeling as more data and information become available.

B. Accountability of PMA Cohort

At the time of database lock, of 955 patients enrolled in PMA study, 63.4% (605) patients are available for analysis at the 6-year follow-up time point.

1. Augmentation, Reconstruction, and Revision Cohorts

The MemoryShape™ Core Study consists of 955 patients (1,831implants) for which data are available through 6 years. The study is divided into 4 cohorts, including 572 primary augmentation patients, 124 revision-augmentation patients, 191 primary reconstruction patients, and 68 revision-reconstruction patients. Data are available through 6 years post-implantation for 69% of the eligible primary augmentation patients, 66% of the eligible revision-augmentation patients, 73% of the eligible primary reconstruction patients, and 76% of the revision- reconstruction patients. Tables 10-13 provide a tabulation of patient accounting by follow-up year and by study cohort.

	10 weeks	1 year	2 years	3 years	4 years	5 years	6 years
Theoretically Due	572	572	572	572	572	572	572
Deaths	0	0	1	1	1	2	2
Discontinued due to explantation	1	6	13	19	21	25	26
Expected	571	566	558	552	550	545	544
Lost to Follow-up	1	5	13	19	30	34	35
Other patients without data	2	19	21	66	93	108	132
Number of patients with Data (% Follow-up)	568 (99%)	542 (96%)	524 (94%)	467 (85%)	427 (78%)	403 (74%)	377 (69%)

Table 10: Patient Accountability for Primary Augmentation Cohort

	10 weeks	1 year	2 years	3 years	4 years	5 years	6 years
Theoretically Due	124	124	124	124	124	124	124
Deaths	0	0	1	1	1	1	1
Discontinued due to explantation	1	4	5	8	9	11	11
Expected	123	120	118	115	114	112	112
Lost to Follow-up	1	3	3	3	5	6	6
Other patients without data	1	0	5	13	25	24	32
Number of patients with Data (% Follow-up)	121 (98%)	117 (98%)	110 (93%)	99 (86%)	84 (74%)	82 (73%)	74 (66%)

Table 11: Patient Accountability for Revision Augmentation Cohort

	10 weeks	1 year	2 years	3 years	4 years	5 years	6 years
Theoretically Due	191	191	191	191	191	194	191
Deaths	0	1	1	2	5	7	7
Discontinued due to explantation	1	5	10	13	17	24	26
Expected	190	185	180	176	169	160	158
Lost to Follow-up	0	0	1	4	7	7	7
Other patients without data	2	5	8	9	19	27	35
Number of patients with Data (% Follow-up)	188 (99%)	180 (97%)	171 (95%)	163 (93%)	143 (85%)	126 (79%)	116 (73%)

Table 12: Patient Accountability for Primary Reconstruction Cohort

	10 weeks	1 year	2 years	3 years	4 years	5 years	6 years
Theoretically Due	68	68	68	68	68	68	68
Deaths	0	0	0	1	1	1	1
Discontinued due to explantation	0	2	5	11	15	16	17
Expected	68	66	63	56	52	51	50
Lost to Follow-up	0	0	1	2	2	4	4
Other patients without data	1	0	0	3	4	5	8
Number of patients with Data (% Follow-up)	67 (99%)	66 (100%)	64 (100%)	51 (91%)	46 (88%)	42 (82%)	38 (76%)

Table 13: Patient Accountability for Revision Reconstruction Cohort

2. MRI Cohort

The MemoryShape™ Core Study MRI cohort originally consisted of 419 patients, including 252 primary augmentation patients, 56 revision-augmentation patients, 74 primary reconstruction patients, and 37 revision-reconstruction patients. The patients enrolled in the MRI cohort were scheduled to have MRIs to screen for silent rupture at 1, 2, 4, 6, 8, and 10 years. On August 3, 2010, the protocol was revised so that all subjects would have MRIs for the remaining 6, 8 and 10 years. Therefore, the number of patients theoretically due at the 6-year time point was changed to 572 primary augmentation patients, 124 revision-augmentation patients, 191 primary reconstruction patients, and 68 revision-reconstruction patients.

For the MRI cohort, data are available through 6 years post-implantation for 56% of the eligible primary augmentation patients, 59% of the eligible revision-augmentation patients, 45% of the eligible primary reconstruction patients, and 71% of

the revision-reconstruction patients. Tables 14-17 present patient accounting for the MRI cohorts by study cohort.

	1 year	2 year	4 year	6 year
All Patients	252	252	252	252
Deaths	0	1	1	1
Discontinuations due to Explantation	3	6	12	15
Expected	249	245	239	236
Lost to Follow-Up	1	6	13	14
Other Patients without Data	63	34	55	90
Number of Patients with Data (% Follow-Up)	185 (74%)	205 (84%)	171 (72%)	132 (56%)

Table 14: MRI Cohort Patient Accountability for MRI Evaluations – Primary Augmentation

	1 year	2 year	4 year	6 year
All Patients	56	56	56	56
Deaths	0	0	0	0
Discontinuations due to Explantation	2	2	5	5
Expected	54	54	51	51
Lost to Follow-Up	1	1	1	1
Other Patients without Data	14	11	13	20
Number of Patients with Data (% Follow-Up)	39 (72%)	42 (78%)	37 (73%)	30 (59%)

Table 15: MRI Cohort Patient Accountability for MRI Evaluations – Revision Augmentation

	1 year	2 year	4 year	6 year
All Patients	74	74	74	74
Deaths	0	0	0	1
Discontinuations due to Explantation	2	6	9	11
Expected	72	68	65	62
Lost to Follow-Up	0	1	4	4
Other Patients without Data	30	11	14	30
Number of Patients with Data (% Follow-Up)	42 (58%)	56 (82%)	47 (72%)	28 (45%)

Table 16: MRI Cohort Patient Accountability for MRI Evaluations – Primary Reconstruction

	1 year	2 year	4 year	6 year
All Patients	37	37	37	37
Deaths	0	0	0	0
Discontinuations due to Explantation	1	1	5	6
Expected	36	36	32	31
Lost to Follow-Up	0	1	1	2
Other Patients without Data	11	4	7	7
Number of Patients with Data (% Follow-Up)	25 (69%)	31 (86%)	24 (75%)	22 (71%)

Table 17: MRI Cohort Patient Accountability for MRI Evaluations – Revision Reconstruction

Tables 18-21 present patient accounting for the non-MRI cohorts by study cohort. In August 2010, a protocol amendment with an FDA-mandated change was made. The amendment specified that "All active patients with study devices will have MRI scans at years 6, 8, and 10". This protocol amendment was implemented during a time that the 6-year visit windows were coming to a close, and therefore, there were only 2 non-MRI cohort patients with 6-year MRIs, and this data set was not sufficient to enable a meaningful Kaplan-Meier analysis. Kaplan-Meier analyses on rupture for the "non-MRI" cohort data after 6 years will be included in future labeling updates.

	1 year	2 year	4 year	6 year
All Patients	320	320	320	320
Deaths	0	0	0	1
Discontinuations due to Explantation	3	7	9	11
Number of Patients with Data	2	1	2	1

Table 18: Non-MRI Cohort Patient Accountability for MRI Evaluations – Primary Augmentation

	1 year	2 year	4 year	6 year
All Patients	68	668	68	68
Deaths	0	1	1	1
Discontinuations due to Explantation	2	3	4	6
Number of Patients with Data	2	1	0	0

Table 19: Non-MRI Cohort Patient Accountability for MRI Evaluations – Revision Augmentation

	1 year	2 year	4 year	6 year
All Patients	117	117	117	117
Deaths	1	1	5	6
Discontinuations due to Explantation	3	4	8	15
Number of Patients with Data	0	1	2	0

Table 20: Non-MRI Cohort Patient Accountability for MRI Evaluations – Primary Reconstruction

	1 year	2 year	4 year	6 year
All Patients	31	31	31	31
Deaths	0	0	1	1
Discontinuations due to Explantation	1	4	10	11
Number of Patients with Data	1	1	1	1

Table 21: Non-MRI Cohort Patient Accountability for MRI Evaluations – Revision Reconstruction

C. Study Population Demographics and Baseline Parameters

Overall, over 90% of the study patients were Caucasian (91% of the primary augmentation patients, 96% for revision-augmentation, 94% of the primary reconstruction patients, and 96% of the revision-reconstruction patients). The median age at surgery was 36 years for primary augmentation patients, 46 for revision-augmentation patients, 47 years for primary reconstruction patients, and 53 years for revision-reconstruction patients. Most of the Mentor MemoryShape™ Core Study patients were married (63% of the primary augmentation patients, 71% for revision-augmentation, 76% of the primary reconstruction patients, and 69% of the revision-reconstruction patients). In addition, the majority of the study patients had some education after high school. Table 22 presents the study patient demographics at baseline by study cohort.

Characteristic	Primary Augmentation N=572	Revision-Augmentation N=124	Primary Reconstruction N=191	Revision-Reconstruction N=68
Age (years)				
<22	32 (5.6%)	1 (0.8%)	3 (1.6%)	0 (0%)
22-<25	32 (5.6%)	0 (0%)	2 (1.0%)	0 (0%)
25-<40	331 (57.9%)	34 (24.7%)	30 (15.7%)	5 (7.4%)
40-<50	150 (26.2%)	45 (36.3%)	85 (44.5%)	21 (30.9%)
50-<60	24 (4.2%)	36 (29.0%)	45 (23.6%)	27 (39.7%)
60-<70	3 (0.5%)	8 (6.5%)	25 (13.1%)	12 (17.6%)

Characteristic	Primary Augmentation N=572	Revision-Augmentation N=124	Primary Reconstruction N=191	Revision-Reconstruction N=68
70 & over	0 (0%)	0 (0%)	1 (0.5%)	3 (4.4%)
Median Age	35 years	46 years	47 years	53 years
Marital Status				
Single	129 (22.6%)	12 (9.7%)	22 (11.5%)	11 (16.2%)
Married	361 (63.1%)	88 (71.0%)	146 (76.4%)	47 (69.1%)
Separated	10 (1.7%)	3 (2.4%)	0 (0%)	1 (1.5%)
Divorced	65 (11.4%)	21 (16.9%)	18 (9.4%)	5 (7.4%)
Widowed	5 (0.9%)	0 (0%)	5 (2.6%)	4 (5.9%)
Not Provided	2 (0.3%)	0 (0%)	0 (0%)	0 (0%)
Race				
Caucasian	518 (90.6%)	119 (96.0%)	179 (93.7%)	65 (95.6%)
African American	6 (1.0%)	0 (0%)	9 (4.7%)	1 (1.5%)
Asian	13 (2.3%)	2 (1.6%)	1 (0.5%)	0 (0%)
Other	30 (5.2%)	3 (2.4%)	2 (1.0%)	1 (1.5%)
Not Provided	5 (0.9%)	0 (0%)	0 (0%)	1 (1.5%)
Education				
Less than 12 years	4 (0.7%)	1 (0.8%)	3 (1.6%)	2 (2.9%)
High School Graduate	48 (8.4%)	15 (12.1%)	25 (13.1%)	9 (13.2%)
Some College	199 (34.8%)	44 (35.5%)	49 (25.7%)	22 (32.4%)
College Graduate	255 (44.6%)	44 (35.5%)	73 (38.2%)	18 (26.5%)
Post Graduate	58 (10.1%)	18 (14.5%)	37 (19.4%)	15 (22.1%)
Not Provided	8 (1.4%)	2 (1.6%)	4 (2.1%)	2 (2.9%)

Table 22: Patient Demographics By Cohort

In the MemoryShape™ Core Study, 1,831 devices (MemoryShape™ textured, medium height, moderate profile breast implant, style MM) were implanted in the 955 study patients. The most common placement location was submuscular/subpectoral (86% for primary augmentation, 67% for revision-augmentation, 93% for primary reconstruction, and 98% for revision- reconstruction). Table 23 presents the placement by study cohort.

Implant Placement	Primary Augmentation N=1143	Revision-Augmentation N=247	Primary Reconstruction N=328	Revision-Reconstruction N=113
Submuscular/Subpectoral	985 (86.2%)	165 (66.8%)	306 (93.3%)	111 (98.2%)
Subglandular	154 (13.5%)	80 (32.4%)	22 (6.7%)	2 (1.8%)
Other[1]	4 (0.3%)	2 (0.8%)	0 (0%)	0 (0%)

[1] The other implant placement positions included partial retro-pectoral (4 primary augmentation patients) and prepectoral (2 revision augmentation patients).

Table 23: Breast Implant Placement by Cohort

With respect to other surgical baseline factors in the MemoryShape™ Core Study, for both primary augmentation and revision-augmentation patients, the most common incision site was inframammary, while for primary reconstruction and revision-reconstruction patients, the most common incision site was the mastectomy scar.

D. Safety and Effectiveness Results

1. Safety Results

The safety analysis was based on data from 955 patients enrolled in the Core study of which 605 patients were available for the 6 year evaluation. The key safety outcomes for this study, including the 6-year cumulative complication rates, reasons for operation, and reasons for implant removal, are presented in tables 20 through 22. Details describing cumulative risk at each follow-up assessment point are presented in table 23. Other clinical safety outcomes are described in bullet (d).

a. 6-year Complication Rates

Table 24 shows 6-year, by-patient, cumulative KM risk rates of first occurrence (95% confidence interval) of complications for all 4 study cohorts. The most commonly experienced complication in all cohorts was reoperation. The incidence rates of reoperation through 6-years were 18% for the primary augmentation cohort, 24% for the revision-augmentation cohort, 45% for the primary reconstruction cohort, and 45% for the revision- reconstruction cohort.

Complications Through 6 Years[1]	Primary Augmentation[2] N=572	Revision-Augmentation[3] N=124	Primary Reconstruction[4] N=191	Revision-Reconstruction[5] N=68
Overall Complications and Reoperations				
Any complication excluding rupture	44.8% (40.6, 49.2)	53.3% (44.5, 62.6)	64.9% (57.9, 71.9)	67.7% (56.0, 78.9)
Any complication excluding cosmetic and rupture	32.2% (28.3, 36.3)	42.1% (33.5, 51.9)	57.1% (49.8, 64.6)	56.1% (44.5, 68.3)
Any complication or reoperation excluding rupture	45.3% (41.2, 49.7)	55.6% (46.8, 64.9)	69.6% (62.8, 76.2)	70.1% (58.5, 80.9)
Any cosmetic complication[6]	21.0% (17.7, 24.8)	27.3% (19.9, 36.7)	24.9% (19.0, 32.2)	36.5% (25.1, 51.0)
Any reoperation	18.1% (15.1, 21.6)	24.1% (17.2, 33.0)	44.5% (37.5, 52.2)	45.4% (34.0, 58.5)
Implant removal with or without replacement	7.0% (5.1, 9.5)	13.6% (8.6, 21.3)	21.8% (16.4, 28.7)	34.2% (24.0, 47.3)
Individual Complications				
Asymmetry	0.7% (0.3, 1.9)	1.7% (0.4, 6.6)	10.6% (6.7, 16.7)	6.1% (2.3, 15.6)
Breast pain	2.4% (1.4, 4.1)	0.9% (0.1, 6.0)	2.8% (1.2, 6.6)	3.3% (0.8, 12.8)
Breast sensation changes	3.6% (2.3, 5.6)	2.7% (0.9, 8.2)	1.1% (0.3, 4.5)	0%
Bruising	0.4% (0.1, 1.4)	0%	0%	0%
Calcification	0.4% (0.1, 1.5)	1.1% (0.2, 7.7)	0%	0%
Capsular contracture Baker II w/surgical intervention	0.6% (0.2, 1.8)	1.7% (0.4, 6.5)	4.2% (2.0, 8.7)	3.7% (0.9, 14.2)
Capsular contracture Baker III, IV	2.4% (1.4, 4.2)	9.7% (5.3, 17.5)	10.1% (6.2, 16.0)	16.4% (8.7, 29.8)
Capsular contracture Baker Grade unknown	0%	0%	0.6% (0.1, 3.9)	0%
Death[7]	0.4% (0.1, 1.6)	0.9% (0.1, 6.2)	4.5% (2.2, 9.3)	1.7% (0.2, 11.6)
Delayed wound healing	0.2% (0.0, 1.2)	1.2% (0.2, 8.5)	1.0% (0.3, 4.1)	0%
Erythema (redness)	0%	0%	0%	1.5% (0.2, 10.0)
Excess skin/tissue	0%	0%	4.3% (2.2, 8.5)	1.6% (0.2, 11.1)
External injury not related to breast implants	0%	0%	0.5% (0.1, 3.7)	0%
Fibrocystic disease	0.7% (0.2, 2.2)	1.2% (0.2, 8.4)	0%	0%
Gel fracture[8]	0%	0%	0%	2.0% (0.3, 13.4)
Granuloma	0.2% (0.0, 1.3)	0%	0%	0%
Hematoma	1.2% (0.6, 2.6)	0%	0%	1.5% (0.2, 10.0)
Hypertrophic scarring	2.5% (1.5, 4.3)	3.4% (1.3, 8.9)	2.4% (0.9, 6.4)	0%
Implant immobility	0%	0%	3.8% (1.7, 8.2)	1.9% (0.3, 12.9)
Implant movement upon muscle contraction	0.6% (0.2, 1.8)	0.9% (0.1, 5.9)	0%	0%
Implant outline visible	0.4% (0.1, 1.6)	0.9% (0.1, 6.2)	0%	0%
Implant rotation	1.1% (0.5, 2.4)	2.6% (0.9, 8.0)	5.1% (2.5, 10.0)	1.5% (0.2, 10.4)
Implant rupture (Based on MRI Cohort)[9]	2.6% (1.0, 6.9)	3.6% (0.5, 22.8)	1.6% (0.2, 11.1)	0%
Infection	0.9% (0.4, 2.1)	2.1% (0.5, 8.7)	1.6% (0.5, 5.0)	3.0% (0.8, 11.4)

Complications Through 6 Years[1]	Primary Augmentation[2] N=572	Revision-Augmentation[3] N=124	Primary Reconstruction[4] N=191	Revision-Reconstruction[5] N=68
Intermittent pop while wearing certain type of bra	0.2% (0.0, 1.4)	0%	0%	0%
Irritation/inflammation	0.9% (0.4, 2.1)	0.8% (0.1, 5.6)	2.1% (0.8, 5.6)	3.0% (0.8, 11.3)
Itching	0%	0%	1.3% (0.3, 5.2)	0%
Lack of projection	0%	1.0% (0.1, 6.6)	8.5% (5.1, 14.1)	13.7% (7.1, 25.6)
Lactation difficulties	0.8% (0.3, 2.1)	0%	0%	0%
Loss of definition of inframammary fold	0.7% (0.3, 1.9)	0%	2.3% (0.9, 6.1)	1.5% (0.2, 10.0)
Mass/cyst	5.9% (4.1, 8.3)	6.6% (3.2, 13.5)	4.6% (2.2, 9.8)	0%
Metastatic disease	0.2% (0.0, 1.3)	0%	2.3% (0.9, 5.9)	1.6% (0.2, 10.9)
Miscarriage	1.6% (0.8, 3.3)	1.1% (0.2, 7.7)	2.1% (0.7, 6.6)	0%
Muscle atrophy	0%	0%	0.6% (0.1, 4.4)	1.5% (0.2, 10.1)
Necrosis	0%	0%	0.5% (0.1, 3.7)	0%
New diagnosis of breast cancer	0.8% (0.3, 2.1)	0.8% (0.1, 5.6)	0.8% (0.1, 5.3)	0%
New diagnosis of Rheumatic disease	1.4% (0.7, 3.0)	0.9% (0.1, 6.0)	1.7% (0.6, 5.1)	0%
Nipple complications	0.3% (0.1, 1.4)	1.1% (0.2, 7.4)	0.6% (0.1, 3.9)	0%
Nipple sensation changes	4.4% (3.0, 6.6)	5.3% (2.4, 11.4)	2.9% (1.2, 6.9)	0%
Other: Missing	0.2% (0.0, 1.4)	0%	1.6% (0.4, 6.3)	0%
Palpability-implant	0.9% (0.4, 2.3)	3.5% (1.3, 9.2)	0.7% (0.1, 5.0)	3.5% (0.9, 13.4)
Paresthesia (numbness/tingling)	0.4% (0.1, 1.6)	0%	0%	3.4% (0.9, 12.9)
Patient dissatisfied with aesthetic appearance of breast	2.8% (1.7, 4.6)	8.1% (4.1, 15.7)	5.1% (2.6, 10.2)	8.4% (3.5, 19.1)
Patient dissatisfied with feel of implant	1.1% (0.5, 2.5)	4.6% (1.9, 10.7)	1.7% (0.6, 5.3)	3.8% (0.9, 14.6)
Patient would not make decision to have breast surgery again	0.6% (0.2, 1.9)	1.2% (0.2, 8.3)	0%	0%
Position dissatisfaction	2.0% (1.1, 3.7)	3.7% (1.4, 9.7)	2.1% (0.7, 6.6)	4.9% (1.6, 14.4)
Ptosis	14.6% (11.7, 18.0)	14.4% (8.7, 23.4)	5.8% (3.0, 10.8)	12.2% (5.5, 25.6)
Rash	0.2% (0.0, 1.3)	0%	0%	0%
Recurrent breast cancer	0%	0%	2.5% (0.9, 6.5)	3.6% (0.9, 13.9)
Scarring	2.4% (1.4, 4.1)	2.2% (0.6, 8.5)	2.9% (1.2, 6.8)	6.5% (2.1, 19.6)
Seroma	0.5% (0.2, 1.7)	0.8% (0.1, 5.9)	3.4% (1.5, 7.4)	4.6% (1.5, 13.5)
Shape distortion	0.5% (0.1, 1.8)	0%	1.6% (0.4, 6.5)	0%
Silicone from previous rupture	0%	0%	0%	1.5% (0.2, 10.0)
Size change-patient request	3.7% (2.4, 5.7)	6.6% (3.4, 12.8)	5.0% (2.6, 9.4)	9.9% (4.5, 20.8)
Size change-physician assessment only	0.2% (0.0, 1.2)	1.7% (0.4, 6.5)	2.1% (0.8, 5.6)	4.8% (1.2, 17.8)
Skin lesion	0.8% (0.3, 2.0)	1.1% (0.2, 7.5)	1.8% (0.6, 5.5)	4.3% (1.1, 16.3)
Suture complication	0.2% (0.0, 1.2)	0.9% (0.1, 5.9)	1.7% (0.6, 5.3)	0%
Swelling (excessive)	0.2% (0.0, 1.2)	0%	0.5% (0.1, 3.7)	1.5% (0.2, 10.0)

Complications Through 6 Years[1]	Primary Augmentation[2] N=572	Revision-Augmentation[3] N=124	Primary Reconstruction[4] N=191	Revision-Reconstruction[5] N=68
Symmastia	0%	0%	0.7% (0.1, 4.9)	0%
Tenderness/soreness	0.8% (0.3, 2.1)	1.3% (0.2, 9.)	1.4% (0.3, 5.7)	0%
Thickened capsule	0.2% (0.0, 1.3)	0.9% (0.1, 6.5)	0%	0%
Wound dehiscence	0.7% (0.3, 1.9)	2.4% (0.8, 7.4)	0.5% (0.1, 3.7)	0%
Wrinkling	2.7% (1.6, 4.5)	5.9% (2.9, 12.0)	4.0% (1.9, 8.2)	12.2% (5.9, 24.5)

[1] Excludes mild occurrences of the following: asymmetry, breast pain, breast sensation changes, calcification, delayed wound healing, nipple sensation changes, position dissatisfaction, nipple complications, wrinkling, and palpability-implant. Also excludes planned second stage surgeries.
[2] 247 primary augmentation patients experienced at least one complication or reoperation
[3] 65 revision-augmentation patients experienced at least one complication or reoperation
[4] 129 primary reconstruction patients experienced at least one complication or reoperation
[5] 46 revision-reconstruction patients experienced at least one complication or reoperation
[6] Cosmetic complications include asymmetry, hypertrophic scarring, ptosis, size-change-patient request, size change-physician assessment only, and wrinkling.
[7] All causes of death were reported by the Investigator to be unrelated to study procedure or device
[8] Gel fracture occurred in 1 revision-reconstruction patient
[9] There were 2 non-MRI patients (1 primary augmentation and 1 revision-augmentation) with a reported rupture. There were only 16 non-MRI cohort patients with MRIs through 6 years, and therefore, there was not sufficient data to conduct Kaplan-Meier analysis on the non-MRI cohort

Table 24: Kaplan-Meier Cumulative Incidence Rates of Occurrence of Complications Through 6 Years

b. Main Reasons for Reoperation

Table 25 shows the main reasons for reoperations through 6 years by study cohort. The rates are based on the total number of reoperations for the study cohort.

Reason for Reoperation through 6 Years[1,2]	Primary Augmentation N=122 Reoperations in 98 Patients	Revision-Augmentation N=36 Reoperations in 28 patients	Primary Reconstruction N=108 Reoperations in 81 patients	Revision-Reconstruction N=36 Reoperations in 29 patients
Asymmetry	5 (4.1%)	2 (5.6%)	13 (12.0%)	3 (8.3%)
Breast mass/cyst	18 (14.8%)	4 (11.1%)	8 (7.4%)	1 (2.8%)
Breast pain	2 (1.6%)	1 (2.8%)	0 (0.0%)	1 (2.8%)
Calcification	8 (6.6%)	1 (2.8%)	1 (0.9%)	0 (0.0%)
Capsular contracture	5 (4.1%)	1 (2.8%)	8 (7.4%)	6 (16.7%)
Delayed wound healing	1 (0.8%)	1 (2.8%)	1 (0.9%)	0 (0.0%)
Excess skin/tissue	1 (0.8%)	0 (0.0%)	6 (5.6%)	1 (2.8%)
Excessive skin along incision	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)
Extrusion	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)
Granuloma	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hematoma/seroma	7 (5.7%)	0 (0.0%)	7 (6.5%)	1 (2.8%)

Reason for Reoperation through 6 Years[1,2]	Primary Augmentation N=122 Reoperations in 98 Patients	Revision-Augmentation N=36 Reoperations in 28 patients	Primary Reconstruction N=108 Reoperations in 81 patients	Revision-Reconstruction N=36 Reoperations in 29 patients
Hypertrophic scarring	8 (6.6%)	1 (2.8%)	0 (0.0%)	0 (0.0%)
Implant immobility	0 (0.0%)	0 (0.0%)	2 (1.9%)	1 (2.8%)
Implant movement upon muscle contraction	1 (0.8%)	1 (2.8%)	0 (0.0%)	0 (0.0%)
Implant rotation	2 (1.6%)	0 (0.0%)	4 (3.7%)	0 (0.0%)
Infection	3 (2.5%)	0 (0.0%)	1 (0.9%)	1 (2.8%)
Irritation/inflammation	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Lack of nipple projection	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)
Lack of projection	0 (0.0%)	0 (0.0%)	5 (4.6%)	3 (8.3%)
Loss of definition of inframammary fold	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
New diagnosis of breast cancer	7 (5.7%)	1 (2.8%)	1 (0.9%)	0 (0.0%)
Nipple complication	2 (1.6%)	0 (0.0%)	0 (0.0%)	4 (11.1%)
Nipple – unacceptably low sensitivity	1 (0.8%)	0 (0.0%)	1 (0.9%)	0 (0.0%)
Patient dissatisfied with aesthetic appearance of breast	2 (1.6%)	1 (2.8%)	2 (1.9%)	2 (5.6%)
Position dissatisfaction	7 (5.7%)	4 (11.1%)	7 (6.5%)	2 (5.6%)
Ptosis	10 (8.2%)	2 (5.6%)	1 (0.9%)	0 (0.0%)
Recurrent breast cancer	0 (0.0%)	0 (0.0%)	2 (1.9%)	1 (2.8%)
Rupture	2 (1.6%)	1 (2.8%)	0 (0.0%)	0 (0.0%)
Scarring	2 (1.6%)	0 (0.0%)	5 (4.6%)	1 (2.8%)
Size change – patient request	15 (12.3%)	3 (8.3%)	4 (3.7%)	3 (8.3%)
Size change – physician assessment only	0 (0.0%)	0 (0.0%)	4 (3.7%)	0 (0.0%)
Skin lesion	2 (1.6%)	2 (5.6%)	1 (0.9%)	1 (2.8%)
Suspected rupture	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)
Suture complication	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)
Upper pole fullness	0 (0.0%)	1 (2.8%)	0 (0.0%)	0 (0.0%)
Wound dehiscence	2 (1.6%)	4 (11.1%)	0 (0.0%)	0 (0.0%)
Wrinkling	2 (1.6%)	4 (11.1%)	5 (4.6%)	3 (8.3%)
Missing	4 (3.3%)	1 (2.8%)	14 (13.0%)	1 (2.8%)

[1]Excludes planned second stage surgeries and reoperations for which the only reason for reoperation was staged reconstruction.

[2] If a bilateral reoperation had different primary reasons for reoperation for the left and right breast implants, a hierarchy of reasons for reoperation was used in order to establish a primary reason for reoperation. In these cases, the following hierarchy was used: Baker III capsular contracture, Baker II capsular contracture w/surgical intervention, breast pain, wrinkling, palpability-implant, asymmetry, ptosis, nipple complication, new diagnosis of

breast cancer, breast mass/cyst, position dissatisfaction, patient dissatisfied with feel of implant, size change-patient request, size change-physician assessment only, and prophylactic mastectomy. These reasons are a complete list for all the cases of bilateral reoperation where a different primary reason for reoperation was given for the left and right breast implants.

Table 25: Main Reasons for Reoperation Through 6 Years

c. Main Reason for Implant Removal

Table 26 shows the main reasons for implant removal through 6 years by study cohort. The rates are based on the total number of explantations for the study cohort and include all implant removals with or without replacement reported up to 72 months post-implant surgery.

Reason for Implant Removal through 6 Years[1,2]	Primary Augmentation N=70 Explants in 37 Patients	Revision-Augmentation N=29 Explants in 16 Patients	Primary Reconstruction N=58 Explants in 39 Patients	Revision-Reconstruction N=36 Explants in 22 Patients
Asymmetry	6 (8.6%)	3 (10.3%)	7 (12.1%)	6 (16.7%)
Breast mass/cyst	0 (0%)	0 (0%)	1 (1.7%)	0 (0%)
Breast pain	0 (0%)	1 (3.4%)	0 (0%)	1 (2.8%)
Capsular contracture	6 (8.6%)	0 (0%)	7 (12.1%)	4 (11.1%)
Extrusion	0 (0%)	0 (0%)	1 (1.7%)	0 (0%)
Hematoma/seroma	0 (0%)	0 (0%)	2 (3.4%)	1 (2.8%)
Implant immobility	0 (0%)	0 (0%)	4 (6.9%)	2 (5.6%)
Implant rotation	2 (2.9%)	0 (0%)	4 (6.9%)	0 (0%)
Infection	0 (0%)	0 (0%)	1 (1.7%)	1 (2.8%)
Lack of projection	0 (0%)	0 (0%)	6 (10.3%)	6 (16.7%)
New diagnosis of breast cancer	3 (4.3%)	2 (6.9%)	1 (1.7%)	0 (0%)
Nipple – unacceptably low sensitivity	0 (0%)	0 (0%)	1 (1.7%)	0 (0%)
Palpability-implant	0 (0%)	0 (0%)	0 (0%)	1 (2.8%)
Patient dissatisfied with aesthetic appearance of breast	4 (5.7%)	2 (6.9%)	2 (3.4%)	1 (2.8%)
Position dissatisfaction	6 (8.6%)	2 (6.9%)	3 (5.2%)	4 (11.1%)
Prophylactic mastectomy	1 (1.4%)	0 (0%)	0 (0%)	0 (0%)
Ptosis	4 (5.7%)	2 (6.9%)	2 (3.4%)	0 (0%)
Recurrent breast cancer	0 (0%)	0 (0%)	0 (0%)	1 (2.8%)
Rupture	2 (2.9%)	1 (3.4%)	0 (0%)	0 (0%)
Size change – patient request	28 (40.0%)	7 (24.1%)	6 (10.3%)	4 (11.1%)
Size change – physician	0 (0%)	1 (3.4%)	4 (6.9%)	0 (0%)

Reason for Implant Removal through 6 Years[1,2]	Primary Augmentation N=70 Explants in 37 Patients	Revision-Augmentation N=29 Explants in 16 Patients	Primary Reconstruction N=58 Explants in 39 Patients	Revision-Reconstruction N=36 Explants in 22 Patients
assessment only				
Upper pole fullness	0 (0%)	2 (6.9%)	0 (0%)	0 (0%)
Wound dehiscence	0 (0%)	1 (3.4%)	0 (0%)	0 (0%)
Wrinkling	4 (5.7%)	5 (17.2%)	3 (5.2%)	4 (11.1%)
Missing	4 (5.7%)	0 (0%)	3 (5.2%)	0 (0%)

[1]Excludes reoperations for which the only reason for reoperation was staged reconstruction, and events after explantation.

Table 26: Main Reason for Implant Removal Through 6 Years

d. Other Clinical Safety Outcomes

Below is a summary of clinical findings from the MemoryShape™ Core Study with regard to the following: connective tissue disease (CTD), CTD signs and symptoms, cancer, anaplastic large cell lymphoma, lactation complications, reproduction complications, and suicide. These issues, along with others, will be evaluated as part of on-going follow-up of patients in the MemoryShape™ Core Study through 10 years post-implantation.

CTD Diagnoses

In the Mentor MemoryShape™ Core Study, there were 7 primary augmentation patients, 1 revision-augmentation patient, and 3 primary reconstruction patients reported to have a new diagnosis of CTD by a rheumatologist. There were no new diagnoses of CTD in the revision-reconstruction cohort. There were 10 diagnoses for the 7 primary augmentation patients: Spondyarthropathies (25 months post implantation), other connective tissue disease (35 months post implantation), Sjögren's syndrome (35 and 42 months post implantation), systemic lupus erythematosus (35, 42, and 44 months post implantation), fibromyalgia (36 and 37 months post implantation), and undifferentiated connective tissue disease (41 months post implantation). There was 1 diagnosis for the revision-augmentation patient: rheumatoid arthritis (11 months post implantation). There were 3 diagnoses for the 3 primary reconstruction patients: rheumatoid arthritis (10 months post implantation), other inflammatory arthritis (11 months post implantation), and other mechanical/degenerative condition (16 months post implantation). It cannot be concluded that these CTD diagnoses were caused by the implants because there was no comparison group of similar women without implants.

CTD Signs and Symptoms

Compared to before having implants, the following significant changes were found in the rheumatologic symptoms and physical examination findings after adjusting for the age effect: decreased night sweats in the primary reconstruction cohort and increased combined pain overall. No significant changes were found in the primary augmentation, revision-augmentation, or revision-reconstruction cohorts. The MemoryShape™ Core Study was not designed to evaluate cause and effect associations because there is no comparison group of women without implants, and because other contributing factors, such as medications and lifestyle/exercise, were not studied. Therefore, it cannot be determined whether these increases were due to the implants or not, based on the MemoryShape™ Core Study.

Cancer

There were four primary augmentation patients and one revision-augmentation patient with new diagnoses of breast cancer through 6 years in Mentor's MemoryShape™ Core Study. As previous breast cancer was an exclusion criteria for augmentation patients, there were no reports of breast cancer reoccurrence in this cohort. For primary reconstruction, four patients had a diagnosis of recurrent breast cancer and one patient had a new diagnosis of breast cancer. Two revision-reconstruction patients had a diagnosis of recurrent breast cancer. No revision-reconstruction patients had a new diagnosis of breast cancer. There were no reports of other new cancers, such as brain, respiratory, or cervical/vulvar in any indication.

Anaplastic Large Cell Lymphoma

Through 6 years, there were no reports of anaplastic large cell lymphoma (ALCL) in any of the patient cohorts.

Lactation Complications

Four of the 44 primary augmentation patients who attempted to breastfeed following breast implantation experienced difficulty with breast feeding through 6 years in Mentor's MemoryShape™ Core Study. All 4 of the revision-augmentation patients who attempted to breastfeed after receiving breast implants had no difficulty. None of the primary reconstruction or revision-reconstruction patients attempted to breastfeed.

Reproduction Complications

Eight primary augmentation patients, one revision-augmentation patient, and three primary reconstruction patients reported a miscarriage. There were no reports of miscarriage in the revision-reconstruction cohort.

Suicide

There were no reports of suicide in any of the four cohorts in Mentor's MemoryShape™ Core Study through 6 years.

e. Cumulative Risk for Occurrence of Each Complication at Each Follow-Up Assessment Point

The cumulative risk for first occurrence of each complication at each follow-up assessment point is presented in table 27. The KM risk rates are presented by study cohort for the 10 week and Year 1 through Year 6 assessment points. The table begins with "Overall Complications and Reoperations" and "Individual Complications" followed by each complication in alphabetical order.

	Study Cohort			
Complication [1,2]	**Primary Augmentation**	**Revision-Augmentation**	**Primary Reconstruction**	**Revision-Reconstruction**
Overall Complications and Reoperations				
Any Complication Excluding Cosmetic and Rupture				
Week 10	7.5%	8.1%	12.6%	8.8%
Year 1	14.2%	19.7%	27.1%	25.2%
Year 2	21.2%	25.7%	34.9%	40.4%
Year 3	26.0%	31.1%	44.1%	49.6%
Year 4	29.8%	36.8%	46.5%	54.4%
Year 5	30.9%	41.0%	54.2%	56.1%
Year 6	32.2%	42.1%	57.1%	56.1%
Any Complication Excluding Rupture				
Week 10	9.1%	12.1%	17.8%	11.8%
Year 1	19.5%	27.7%	32.6%	32.6%
Year 2	28.1%	35.1%	44.4%	46.3%
Year 3	35.0%	41.0%	54.4%	55.5%
Year 4	40.4%	49.2%	56.7%	58.8%
Year 5	42.1%	52.2%	62.2%	63.9%
Year 6	44.8%	53.3%	64.9%	67.7%
Any Complication or Reoperation Excluding Rupture				
Week 10	9.3%	12.9%	18.9%	11.8%
Year 1	20.0%	28.5%	38.4%	33.8%
Year 2	28.9%	35.9%	50.6%	47.3%
Year 3	35.6%	43.5%	59.3%	56.3%
Year 4	41.0%	51.6%	62.8%	59.5%

Complication [1,2]	Study Cohort			
	Primary Augmentation	**Revision-Augmentation**	**Primary Reconstruction**	**Revision-Reconstruction**
Year 5	42.6%	54.6%	67.0%	64.5%
Year 6	45.3%	55.6%	69.6%	70.1%
Any Cosmetic Complication				
Week 10	2.1%	5.7%	6.8%	4.4%
Year 1	6.7%	14.8%	9.5%	13.3%
Year 2	10.1%	17.3%	15.0%	17.9%
Year 3	14.4%	19.0%	16.7%	23.1%
Year 4	17.5%	23.8%	19.9%	23.1%
Year 5	19.0%	24.8%	21.9%	29.4%
Year 6	21.0%	27.3%	24.9%	36.5%
Any Reoperation				
Week 10	3.5%	2.4%	4.7%	0%
Year 1	6.5%	9.0%	22.1%	8.8%
Year 2	10.4%	13.9%	30.1%	17.7%
Year 3	13.6%	18.2%	36.1%	28.4%
Year 4	15.7%	21.0%	39.6%	36.6%
Year 5	17.2%	24.1%	42.2%	41.8%
Year 6	18.1%	24.1%	44.5%	45.4%
Implant Removal with or without Replacement				
Week 10	0.3%	0.8%	2.1%	0%
Year 1	1.6%	5.7%	7.9%	5.9%
Year 2	3.6%	7.4%	10.6%	11.9%
Year 3	5.0%	10.8%	13.8%	21.0%
Year 4	5.6%	12.6%	17.3%	29.0%
Year 5	6.3%	13.6%	21.1%	30.6%
Year 6	7.0%	13.6%	21.8%	34.2%
Individual Complications				
Asymmetry				
Week 10	0.2%	0%	2.1%	1.5%
Year 1	0.5%	1.7%	4.2%	4.5%
Year 2	0.5%	1.7%	6.0%	4.5%
Year 3	0.7%	1.7%	6.0%	6.1%
Year 4	0.7%	1.7%	6.0%	6.1%
Year 5	0.7%	1.7%	7.4%	6.1%
Year 6	0.7%	1.7%	10.6%	6.1%
Breast Sensation Changes				
Week 10	1.0%	0.8%	0.5%	0%
Year 1	1.9%	0.8%	0.5%	0%
Year 2	2.3%	0.8%	0.5%	0%
Year 3	2.7%	2.7%	1.1%	0%
Year 4	3.3%	2.7%	1.1%	0%
Year 5	3.3%	2.7%	1.1%	0%

Complication [1,2]	Study Cohort			
	Primary Augmentation	Revision-Augmentation	Primary Reconstruction	Revision-Reconstruction
Year 6	3.6%	2.7%	1.1%	0%
Breast pain				
Week 10	0.7%	0%	0.5%	0%
Year 1	1.2%	0.9%	1.6%	1.5%
Year 2	1.8%	0.9%	2.2%	1.5%
Year 3	2.2%	0.9%	2.8%	3.3%
Year 4	2.4%	0.9%	2.8%	3.3%
Year 5	2.4%	0.9%	2.8%	3.3%
Year 6	2.4%	0.9%	2.8%	3.3%
Bruising				
Week 10	0%	0%	0%	0%
Year 1	0.2%	0%	0%	0%
Year 2	0.4%	0%	0%	0%
Year 3	0.4%	0%	0%	0%
Year 4	0.4%	0%	0%	0%
Year 5	0.4%	0%	0%	0%
Year 6	0.4%	0%	0%	0%
Calcification				
Week 10	0%	0%	0%	0%
Year 1	0%	0%	0%	0%
Year 2	0.2%	0%	0%	0%
Year 3	0.2%	0%	0%	0%
Year 4	0.4%	0%	0%	0%
Year 5	0.4%	1.1%	0%	0%
Year 6	0.4%	1.1%	0%	0%
Capsular Contracture Baker II w/ Surgical Intervention				
Week 10	0%	0.8%	0%	0%
Year 1	0%	1.7%	1.1%	1.5%
Year 2	0.2%	1.7%	1.1%	1.5%
Year 3	0.6%	1.7%	1.7%	1.5%
Year 4	0.6%	1.7%	4.2%	3.7%
Year 5	0.6%	1.7%	4.2%	3.7%
Year 6	0.6%	1.7%	4.2%	3.7%
Capsular Contracture Baker III, IV				
Week 10	0%	0%	1.6%	2.9%
Year 1	0.4%	3.4%	3.2%	2.9%
Year 2	0.7%	5.2%	3.2%	6.1%
Year 3	1.1%	5.2%	5.6%	13.5%
Year 4	1.5%	8.3%	6.2%	13.5%
Year 5	2.4%	8.3%	7.6%	13.5%
Year 6	2.4%	9.7%	10.1%	16.4%
Capsular Contracture Baker Grade Unknown				

Complication [1,2]	Study Cohort			
	Primary Augmentation	Revision-Augmentation	Primary Reconstruction	Revision-Reconstruction
Week 10	0%	0%	0%	0%
Year 1	0%	0%	0%	0%
Year 2	0%	0%	0.6%	0%
Year 3	0%	0%	0.6%	0%
Year 4	0%	0%	0.6%	0%
Year 5	0%	0%	0.6%	0%
Year 6	0%	0%	0.6%	0%
Death[3]				
Week 10	0%	0%	0%	0%
Year 1	0%	0%	0.5%	0%
Year 2	0.2%	0.9%	0.5%	0%
Year 3	0.2%	0.9%	1.1%	1.7%
Year 4	0.2%	0.9%	3.1%	1.7%
Year 5	0.4%	0.9%	4.5%	1.7%
Year 6	0.4%	0.9%	4.5%	1.7%
Delayed Wound Healing				
Week 10	0.2%	0%	1.0%	0%
Year 1	0.2%	0%	1.0%	0%
Year 2	0.2%	0%	1.0%	0%
Year 3	0.2%	0%	1.0%	0%
Year 4	0.2%	0%	1.0%	0%
Year 5	0.2%	0%	1.0%	0%
Year 6	0.2%	1.2%	1.0%	0%
Erythema (redness)				
Week 10	0%	0%	0%	1.5%
Year 1	0%	0%	0%	1.5%
Year 2	0%	0%	0%	1.5%
Year 3	0%	0%	0%	1.5%
Year 4	0%	0%	0%	1.5%
Year 5	0%	0%	0%	1.5%
Year 6	0%	0%	0%	1.5%
Excess Skin/tissue				
Week 10	0%	0%	1.6%	0%
Year 1	0%	0%	3.8%	0%
Year 2	0%	0%	4.3%	1.6%
Year 3	0%	0%	4.3%	1.6%
Year 4	0%	0%	4.3%	1.6%
Year 5	0%	0%	4.3%	1.6%
Year 6	0%	0%	4.3%	1.6%
External Injury Not Related To Breast Implants				
Week 10	0%	0%	0.5%	0%
Year 1	0%	0%	0.5%	0%
Year 2	0%	0%	0.5%	0%
Year 3	0%	0%	0.5%	0%

Complication [1,2]	Study Cohort			
	Primary Augmentation	Revision-Augmentation	Primary Reconstruction	Revision-Reconstruction
Year 4	0%	0%	0.5%	0%
Year 5	0%	0%	0.5%	0%
Year 6	0%	0%	0.5%	0%
Fibrocystic Disease				
Week 10	0%	0%	0%	0%
Year 1	0%	0%	0%	0%
Year 2	0%	0%	0%	0%
Year 3	0.2%	0%	0%	0%
Year 4	0.2%	0%	0%	0%
Year 5	0.4%	0%	0%	0%
Year 6	0.7%	1.2%	0%	0%
Gel Fracture[4]				
Week 10	0%	0%	0%	0%
Year 1	0%	0%	0%	0%
Year 2	0%	0%	0%	0%
Year 3	0%	0%	0%	0%
Year 4	0%	0%	0%	2.0%
Year 5	0%	0%	0%	2.0%
Year 6	0%	0%	0%	2.0%
Granuloma				
Week 10	0%	0%	0%	0%
Year 1	0.2%	0%	0%	0%
Year 2	0.2%	0%	0%	0%
Year 3	0.2%	0%	0%	0%
Year 4	0.2%	0%	0%	0%
Year 5	0.2%	0%	0%	0%
Year 6	0.2%	0%	0%	0%
Hematoma				
Week 10	1.2%	0%	0%	0%
Year 1	1.2%	0%	0%	1.5%
Year 2	1.2%	0%	0%	1.5%
Year 3	1.2%	0%	0%	1.5%
Year 4	1.2%	0%	0%	1.5%
Year 5	1.2%	0%	0%	1.5%
Year 6	1.2%	0%	0%	1.5%
Hypertrophic Scarring				
Week 10	0%	0.8%	0.5%	0%
Year 1	1.4%	1.7%	1.1%	0%
Year 2	2.2%	3.4%	1.1%	0%
Year 3	2.5%	3.4%	1.1%	0%
Year 4	2.5%	3.4%	2.4%	0%
Year 5	2.5%	3.4%	2.4%	0%
Year 6	2.5%	3.4%	2.4%	0%
Implant Immobility				

Complication [1,2]	Study Cohort			
	Primary Augmentation	**Revision-Augmentation**	**Primary Reconstruction**	**Revision-Reconstruction**
Week 10	0%	0%	0%	0%
Year 1	0%	0%	0%	0%
Year 2	0%	0%	0.6%	0%
Year 3	0%	0%	2.4%	1.9%
Year 4	0%	0%	3.8%	1.9%
Year 5	0%	0%	3.8%	1.9%
Year 6	0%	0%	3.8%	1.9%
Implant Movement Upon Muscle Contraction				
Week 10	0%	0%	0%	0%
Year 1	0.4%	0.9%	0%	0%
Year 2	0.4%	0.9%	0%	0%
Year 3	0.4%	0.9%	0%	0%
Year 4	0.4%	0.9%	0%	0%
Year 5	0.6%	0.9%	0%	0%
Year 6	0.6%	0.9%	0%	0%
Implant Outline Visible Through Skin				
Week 10	0%	0%	0%	0%
Year 1	0.2%	0%	0%	0%
Year 2	0.2%	0.9%	0%	0%
Year 3	0.2%	0.9%	0%	0%
Year 4	0.4%	0.9%	0%	0%
Year 5	0.4%	0.9%	0%	0%
Year 6	0.4%	0.9%	0%	0%
Implant Rotation				
Week 10	0.3%	0.8%	0%	0%
Year 1	0.3%	0.8%	1.1%	1.5%
Year 2	1.1%	1.7%	2.2%	1.5%
Year 3	1.1%	2.6%	3.4%	1.5%
Year 4	1.1%	2.6%	3.4%	1.5%
Year 5	1.1%	2.6%	4.2%	1.5%
Year 6	1.1%	2.6%	5.1%	1.5%
Implant Rupture (Based on the MRI Cohort)[5]				
Year 1	0%	0%	1.6%	0%
Year 2	0%	0%	1.6%	0%
Year 4	1.1%	0%	1.6%	0%
Year 6	2.6%	3.6%	1.6%	0%
Infection				
Week 10	0.7%	0.8%	1.0%	1.5%
Year 1	0.7%	0.8%	1.0%	3.0%
Year 2	0.7%	0.8%	1.0%	3.0%
Year 3	0.9%	0.8%	1.6%	3.0%
Year 4	0.9%	0.8%	1.6%	3.0%

Complication [1,2]	Study Cohort			
	Primary Augmentation	**Revision-Augmentation**	**Primary Reconstruction**	**Revision-Reconstruction**
Year 5	0.9%	0.8%	1.6%	3.0%
Year 6	0.9%	2.1%	1.6%	3.0%
Intermittent Pop While Wearing a Certain Type of Bra				
Week 10	0%	0%	0%	0%
Year 1	0%	0%	0%	0%
Year 2	0%	0%	0%	0%
Year 3	0.2%	0%	0%	0%
Year 4	0.2%	0%	0%	0%
Year 5	0.2%	0%	0%	0%
Year 6	0.2%	0%	0%	0%
Irritation/Inflammation				
Week 10	0.3%	0.8%	1.0%	1.5%
Year 1	0.9%	0.8%	2.1%	3.0%
Year 2	0.9%	0.8%	2.1%	3.0%
Year 3	0.9%	0.8%	2.1%	3.0%
Year 4	0.9%	0.8%	2.1%	3.0%
Year 5	0.9%	0.8%	2.1%	3.0%
Year 6	0.9%	0.8%	2.1%	3.0%
Itching				
Week 10	0%	0%	0.5%	0%
Year 1	0%	0%	0.5%	0%
Year 2	0%	0%	0.5%	0%
Year 3	0%	0%	0.5%	0%
Year 4	0%	0%	0.5%	0%
Year 5	0%	0%	1.3%	0%
Year 6	0%	0%	1.3%	0%
Lack of Projection				
Week 10	0%	0%	1.6%	0%
Year 1	0%	0%	2.7%	0%
Year 2	0%	0%	2.7%	6.3%
Year 3	0%	1.0%	5.0%	11.8%
Year 4	0%	1.0%	7.0%	13.7%
Year 5	0%	1.0%	8.5%	13.7%
Year 6	0%	1.0%	8.5%	13.7%
Lactation Difficulties				
Week 10	0%	0%	0%	0%
Year 1	0%	0%	0%	0%
Year 2	0.2%	0%	0%	0%
Year 3	0.6%	0%	0%	0%
Year 4	0.6%	0%	0%	0%
Year 5	0.8%	0%	0%	0%
Year 6	0.8%	0%	0%	0%

	Study Cohort			
Complication [1,2]	**Primary Augmentation**	**Revision-Augmentation**	**Primary Reconstruction**	**Revision-Reconstruction**
Loss of Definition of Inframammary Fold				
Week 10	0.2%	0%	0%	0%
Year 1	0.2%	0%	1.1%	1.5%
Year 2	0.7%	0%	1.7%	1.5%
Year 3	0.7%	0%	1.7%	1.5%
Year 4	0.7%	0%	2.3%	1.5%
Year 5	0.7%	0%	2.3%	1.5%
Year 6	0.7%	0%	2.3%	1.5%
Mass/cyst				
Week 10	0.2%	0%	0.5%	0%
Year 1	0.7%	0.8%	1.1%	0%
Year 2	2.5%	2.6%	2.2%	0%
Year 3	3.7%	5.4%	2.8%	0%
Year 4	5.4%	5.4%	2.8%	0%
Year 5	5.4%	6.6%	3.6%	0%
Year 6	5.9%	6.6%	4.6%	0%
Metastatic Disease				
Week 10	0%	0%	0%	0%
Year 1	0%	0%	1.7%	0%
Year 2	0.2%	0%	1.7%	1.6%
Year 3	0.2%	0%	2.3%	1.6%
Year 4	0.2%	0%	2.3%	1.6%
Year 5	0.2%	0%	2.3%	1.6%
Year 6	0.2%	0%	2.3%	1.6%
Miscarriage				
Week 10	0%	0%	0%	0%
Year 1	0%	0%	0%	0%
Year 2	0.4%	0%	0%	0%
Year 3	0.8%	0%	0.6%	0%
Year 4	1.4%	0%	1.3%	0%
Year 5	1.4%	1.1%	1.3%	0%
Year 6	1.6%	1.1%	2.1%	0%
Muscle Atrophy				
Week 10	0%	0%	0%	0%
Year 1	0%	0%	0%	1.5%
Year 2	0%	0%	0%	1.5%
Year 3	0%	0%	0%	1.5%
Year 4	0%	0%	0.6%	1.5%
Year 5	0%	0%	0.6%	1.5%
Year 6	0%	0%	0.6%	1.5%
Necrosis				
Week 10	0%	0%	0.5%	0%
Year 1	0%	0%	0.5%	0%
Year 2	0%	0%	0.5%	0%

Complication [1,2]	Study Cohort			
	Primary Augmentation	Revision-Augmentation	Primary Reconstruction	Revision-Reconstruction
Year 3	0%	0%	0.5%	0%
Year 4	0%	0%	0.5%	0%
Year 5	0%	0%	0.5%	0%
Year 6	0%	0%	0.5%	0%
New Diagnosis of Breast Cancer				
Week 10	0%	0.8%	0%	0%
Year 1	0.2%	0.8%	0%	0%
Year 2	0.4%	0.8%	0%	0%
Year 3	0.4%	0.8%	0%	0%
Year 4	0.6%	0.8%	0%	0%
Year 5	0.8%	0.8%	0.8%	0%
Year 6	0.8%	0.8%	0.8%	0%
New Diagnosis of Rheumatic Disease				
Week 10	0%	0%	0%	0%
Year 1	0%	0.9%	1.1%	0%
Year 2	0%	0.9%	1.7%	0%
Year 3	0.4%	0.9%	1.7%	0%
Year 4	1.4%	0.9%	1.7%	0%
Year 5	1.4%	0.9%	1.7%	0%
Year 6	1.4%	0.9%	1.7%	0%
Nipple Complication				
Week 10	0.3%	0%	0%	0%
Year 1	0.3%	0%	0%	0%
Year 2	0.3%	0%	0.6%	0%
Year 3	0.3%	0%	0.6%	0%
Year 4	0.3%	1.1%	0.6%	0%
Year 5	0.3%	1.1%	0.6%	0%
Year 6	0.3%	1.1%	0.6%	0%
Nipple Sensation Changes				
Week 10	1.4%	0.8%	0.5%	0%
Year 1	2.5%	2.5%	0.5%	0%
Year 2	3.5%	3.4%	1.7%	0%
Year 3	3.7%	5.3%	2.3%	0%
Year 4	4.2%	5.3%	2.9%	0%
Year 5	4.2%	5.3%	2.9%	0%
Year 6	4.4%	5.3%	2.9%	0%
Other: Missing				
Week 10	0%	0%	0%	0%
Year 1	0%	0%	0%	0%
Year 2	0%	0%	0%	0%
Year 3	0.2%	0%	0%	0%
Year 4	0.2%	0%	0%	0%
Year 5	0.2%	0%	0.7%	0%

	Study Cohort			
Complication [1,2]	**Primary Augmentation**	**Revision-Augmentation**	**Primary Reconstruction**	**Revision-Reconstruction**
Year 6	0.2%	0%	1.6%	0%
Palpability-Implant				
Week 10	0%	0.8%	0%	0%
Year 1	0.4%	1.7%	0%	0%
Year 2	0.7%	2.6%	0%	1.6%
Year 3	0.7%	2.6%	0%	3.5%
Year 4	0.7%	3.5%	0%	3.5%
Year 5	0.9%	3.5%	0.7%	3.5%
Year 6	0.9%	3.5%	0.7%	3.5%
Paresthesia (numbness/tingling)				
Week 10	0%	0%	0%	0%
Year 1	0%	0%	0%	1.5%
Year 2	0%	0%	0%	1.5%
Year 3	0.2%	0%	0%	3.4%
Year 4	0.4%	0%	0%	3.4%
Year 5	0.4%	0%	0%	3.4%
Year 6	0.4%	0%	0%	3.4%
Patient Dissatisfied with Aesthetic Appearance of Breast				
Week 10	0.4%	0%	0.5%	0%
Year 1	1.2%	2.6%	1.6%	1.5%
Year 2	2.0%	2.6%	2.2%	6.3%
Year 3	2.2%	2.6%	2.2%	6.3%
Year 4	2.8%	5.6%	3.5%	8.4%
Year 5	2.8%	6.7%	4.2%	8.4%
Year 6	2.8%	8.1%	5.1%	8.4%
Patient Dissatisfied with Feel of Implant				
Week 10	0%	0.8%	0.5%	0%
Year 1	0.4%	3.4%	0.5%	1.5%
Year 2	0.9%	3.4%	0.5%	1.5%
Year 3	0.9%	3.4%	1.7%	1.5%
Year 4	1.1%	3.4%	1.7%	1.5%
Year 5	1.1%	4.6%	1.7%	3.8%
Year 6	1.1%	4.6%	1.7%	3.8%
Patient Would Not Make Decision to Have Breast Surgery Again				
Week 10	0%	0%	0%	0%
Year 1	0%	0%	0%	0%
Year 2	0.2%	0%	0%	0%
Year 3	0.4%	0%	0%	0%
Year 4	0.4%	0%	0%	0%

Complication [1,2]	Study Cohort			
	Primary Augmentation	Revision-Augmentation	Primary Reconstruction	Revision-Reconstruction
Year 5	0.4%	0%	0%	0%
Year 6	0.6%	1.2%	0%	0%
Position Dissatisfaction				
Week 10	0.2%	0%	0%	0%
Year 1	0.7%	0.8%	0.5%	0%
Year 2	1.4%	1.7%	0.5%	3.2%
Year 3	1.8%	2.7%	0.5%	4.9%
Year 4	1.8%	3.7%	0.5%	4.9%
Year 5	2.0%	3.7%	1.3%	4.9%
Year 6	2.0%	3.7%	2.1%	4.9%
Ptosis				
Week 10	0.7%	0%	0%	1.5%
Year 1	3.0%	2.5%	0.6%	1.5%
Year 2	4.6%	3.4%	2.3%	3.1%
Year 3	7.9%	5.3%	2.9%	5.0%
Year 4	10.7%	9.4%	4.2%	7.1%
Year 5	12.3%	10.6%	4.9%	7.1%
Year 6	14.6%	14.4%	5.8%	12.2%
Rash				
Week 10	0%	0%	0%	0%
Year 1	0%	0%	0%	0%
Year 2	0.2%	0%	0%	0%
Year 3	0.2%	0%	0%	0%
Year 4	0.2%	0%	0%	0%
Year 5	0.2%	0%	0%	0%
Year 6	0.2%	0%	0%	0%
Recurrent Breast Cancer				
Week 10	0%	0%	0%	0%
Year 1	0%	0%	0.6%	1.5%
Year 2	0%	0%	1.1%	1.5%
Year 3	0%	0%	1.7%	1.5%
Year 4	0%	0%	1.7%	3.6%
Year 5	0%	0%	2.5%	3.6%
Year 6	0%	0%	2.5%	3.6%
Scarring				
Week 10	0.7%	0%	0%	0%
Year 1	1.2%	0%	1.1%	1.5%
Year 2	1.6%	0%	2.3%	1.5%
Year 3	2.2%	0%	2.9%	1.5%
Year 4	2.2%	1.0%	2.9%	3.6%
Year 5	2.4%	2.2%	2.9%	3.6%
Year 6	2.4%	2.2%	2.9%	6.5%
Seroma				
Week 10	0.3%	0%	2.1%	2.9%

Complication [1,2]	Study Cohort			
	Primary Augmentation	Revision-Augmentation	Primary Reconstruction	Revision-Reconstruction
Year 1	0.3%	0.8%	2.1%	2.9%
Year 2	0.5%	0.8%	2.1%	4.6%
Year 3	0.5%	0.8%	2.7%	4.6%
Year 4	0.5%	0.8%	2.7%	4.6%
Year 5	0.5%	0.8%	3.4%	4.6%
Year 6	0.5%	0.8%	3.4%	4.6%
Shape Distortion				
Week 10	0%	0%	0%	0%
Year 1	0%	0%	0%	0%
Year 2	0%	0%	0%	0%
Year 3	0%	0%	0%	0%
Year 4	0%	0%	0%	0%
Year 5	0.2%	0%	0.8%	0%
Year 6	0.5%	0%	1.6%	0%
Silicone From Previous Rupture				
Week 10	0%	0%	0%	1.5%
Year 1	0%	0%	0%	1.5%
Year 2	0%	0%	0%	1.5%
Year 3	0%	0%	0%	1.5%
Year 4	0%	0%	0%	1.5%
Year 5	0%	0%	0%	1.5%
Year 6	0%	0%	0%	1.5%
Size Change-Patient Request				
Week 10	0.7%	2.4%	1.6%	0%
Year 1	1.2%	5.8%	2.1%	4.4%
Year 2	2.5%	6.6%	3.8%	6.0%
Year 3	3.3%	6.6%	5.0%	7.8%
Year 4	3.3%	6.6%	5.0%	7.8%
Year 5	3.5%	6.6%	5.0%	9.9%
Year 6	3.7%	6.6%	5.0%	9.9%
Size Change-Physician Assessment only				
Week 10	0.2%	0.8%	1.6%	0%
Year 1	0.2%	1.7%	1.6%	0%
Year 2	0.2%	1.7%	1.6%	0%
Year 3	0.2%	1.7%	2.1%	0%
Year 4	0.2%	1.7%	2.1%	0%
Year 5	0.2%	1.7%	2.1%	4.8%
Year 6	0.2%	1.7%	2.1%	4.8%
Skin Lesion				
Week 10	0.2%	0%	0.5%	0%
Year 1	0.2%	0%	1.1%	0%
Year 2	0.5%	0%	1.1%	0%

Complication [1,2]	Study Cohort			
	Primary Augmentation	Revision-Augmentation	Primary Reconstruction	Revision-Reconstruction
Year 3	0.5%	0%	1.1%	1.8%
Year 4	0.5%	0%	1.1%	1.8%
Year 5	0.8%	1.1%	1.8%	4.3%
Year 6	0.8%	1.1%	1.8%	4.3%
Suture Complication				
Week 10	0.2%	0%	0%	0%
Year 1	0.2%	0.9%	0.5%	0%
Year 2	0.2%	0.9%	1.1%	0%
Year 3	0.2%	0.9%	1.7%	0%
Year 4	0.2%	0.9%	1.7%	0%
Year 5	0.2%	0.9%	1.7%	0%
Year 6	0.2%	0.9%	1.7%	0%
Swelling (Excessive)				
Week 10	0.2%	0%	0.5%	1.5%
Year 1	0.2%	0%	0.5%	1.5%
Year 2	0.2%	0%	0.5%	1.5%
Year 3	0.2%	0%	0.5%	1.5%
Year 4	0.2%	0%	0.5%	1.5%
Year 5	0.2%	0%	0.5%	1.5%
Year 6	0.2%	0%	0.5%	1.5%
Symmastia				
Week 10	0%	0%	0%	0%
Year 1	0%	0%	0%	0%
Year 2	0%	0%	0%	0%
Year 3	0%	0%	0%	0%
Year 4	0%	0%	0%	0%
Year 5	0%	0%	0.7%	0%
Year 6	0%	0%	0.7%	0%
Tenderness/ Soreness				
Week 10	0.2%	0%	0%	0%
Year 1	0.4%	0%	0.5%	0%
Year 2	0.4%	0%	0.5%	0%
Year 3	0.4%	0%	0.5%	0%
Year 4	0.6%	0%	0.5%	0%
Year 5	0.6%	0%	0.5%	0%
Year 6	0.8%	1.3%	1.4%	0%
Thickened Capsule				
Week 10	0%	0%	0%	0%
Year 1	0.2%	0%	0%	0%
Year 2	0.2%	0%	0%	0%
Year 3	0.2%	0.9%	0%	0%
Year 4	0.2%	0.9%	0%	0%
Year 5	0.2%	0.9%	0%	0%
Year 6	0.2%	0.9%	0%	0%
Wound Dehiscence				

Complication [1,2]	Study Cohort			
	Primary Augmentation	Revision-Augmentation	Primary Reconstruction	Revision-Reconstruction
Week 10	0.7%	1.6%	0.5%	0%
Year 1	0.7%	2.4%	0.5%	0%
Year 2	0.7%	2.4%	0.5%	0%
Year 3	0.7%	2.4%	0.5%	0%
Year 4	0.7%	2.4%	0.5%	0%
Year 5	0.7%	2.4%	0.5%	0%
Year 6	0.7%	2.4%	0.5%	0%
Wrinkling				
Week 10	0.5%	2.4%	1.6%	1.5%
Year 1	1.2%	4.9%	2.1%	4.5%
Year 2	1.6%	4.9%	3.3%	7.6%
Year 3	1.8%	4.9%	3.3%	9.5%
Year 4	2.4%	5.9%	4.0%	9.5%
Year 5	2.4%	5.9%	4.0%	9.5%
Year 6	2.7%	5.9%	4.0%	12.2%

[1] Excludes mild occurrences of the following: asymmetry, breast pain, breast sensation changes, calcification, delayed wound healing, nipple sensation changes, position dissatisfaction, nipple complications, wrinkling, and palpability-implant.

[2] Cosmetic complications include asymmetry, hypertrophic scarring, ptosis, size-change-patient request, size change-physician assessment only, and wrinkling.

[3] All causes of death were reported by the Investigator to be unrelated to study procedure or device.

[4] Gel fracture occurred in 1 revision-reconstruction patient.

[5] There were 2 non-MRI patients (1 primary augmentation and 1 revision-augmentation) with a reported rupture. There were only 16 non-MRI cohort patients with MRIs through 6 years, and therefore, there was not sufficient data to conduct Kaplan-Meier analysis on the non-MRI cohort.

Table 27: KM Risk Rates (95% CI) Through 6 Years for All Time Points

2. Effectiveness Results

The analysis of effectiveness was based on the 605 evaluable patients at the 6 year time point.

Effectiveness was assessed by bra cup size change (primary augmentation patients only), circumferential chest size change, patient satisfaction, and QoL (self-worth, body image, physical, mental, and social health, and breast satisfaction). Patient satisfaction was based on a single question of "Would the subject make the same decision to have this breast surgery?". The QoL measures were the Rosenberg Self Esteem Scale (measures self-worth or self-acceptance), the Body Esteem Scale (measures a person's body image), the SF-36 (measures physical, mental and social health), and the Breast Evaluation Questionnaire (measures breast

satisfaction). These outcomes were assessed before implantation and at 1, 2, 4, and 6 year time points.

Primary Augmentation Patients

For primary augmentation patients, 364 (64%) out of the 572 patients enrolled were included in the analysis of cup size at 6 years. Of these 364 patients, 352 (97%) experienced at least one cup size increase. For circumferential chest size, 366 (64%) of the 572 patients enrolled were included in the analysis at 6 years. The average increase in circumferential chest size was 5.3 centimeters (2.1 inches).

At 6 years, 373 (65%) of the 572 patients enrolled answered the patient satisfaction question. Of these 373 patients, 360 (97%) stated to their surgeon that they would make the same decision to have breast surgery.

With regard to QoL measures at 6 years for primary augmentation patients, there was no significant change in the SF-36. There was a significant increase in the total score and the positive attitude score for the Rosenberg Self Esteem Scale and the total score and chest and sexual attractiveness subscales for the Body Esteem Scale. Of the 356 primary augmentation patients that answered the question "How satisfied with the general appearance of your breasts are you?"; 254 (71%) were very satisfied, 71 (20%) were somewhat satisfied, 8 (2%) were neither satisfied nor dissatisfied, 19 (5%) were somewhat dissatisfied and 4 (1%) were very dissatisfied. Based on the Breast Evaluation Questionnaire, the average improvement from before getting implants was 62% for comfort when not fully dressed, 25% for comfort when fully dressed, and 86% for satisfaction with breast characteristics.

Revision-Augmentation Patients

For revision-augmentation patients, 70 (56%) out of the 124 patients enrolled were included in the circumferential chest size analysis at 6 years. The average increase in circumferential chest size was 1.8 centimeters (0.7 inches).

At 6 years, 73 (59%) of the 124 revision-augmentation patients enrolled answered the patient satisfaction question. Of these 73 patients, 69 (95%) stated to their surgeon that they would make the same decision to have breast surgery.

With regard to QoL measures at 6 years for revision-augmentation patients, there was no significant change in the SF-36 or Rosenberg Self Esteem Scale. For the Body Esteem Scale, there was a significant decrease in the total score and an increase in chest subscale. Of the 68 revision-augmentation patients that answered

the question "How satisfied with the general appearance of your breasts are you?"; 29 (43%) were very satisfied, 27 (40%) were somewhat satisfied, 8 (12%) were somewhat dissatisfied and 4 (6%) were very dissatisfied. Based on the Breast Evaluation Questionnaire, the average improvement from before getting implants was 11% for comfort when not fully dressed, 5% for comfort when fully dressed, and 28% for satisfaction with breast characteristics.

Primary Reconstruction Patients

For primary reconstruction patients, 85 (45%) out of the 191 patients enrolled were included in the analysis of circumferential chest size at 6 years. The average increase in circumferential chest size was 0.8 centimeters (0.3 inches).

At 6 years, 99 (52%) of 191 primary reconstruction patients enrolled answered the patient satisfaction question. Of these 99 patients, 97 (98%) stated to their surgeon that they would make the same decision to have breast surgery.

With regard to QoL measures at 6 years for primary reconstruction patients, there was a significant increase for the physical component scores but no significant change in the mental component score of the SF-36. There was a significant decrease in the total score of the Rosenberg Self Esteem Scale. For the Body Esteem Scale, there was a significant increase in the chest subscale. Of the 106 primary reconstruction patients that answered the question "How satisfied with the general appearance of your breasts are you?"; 39 (37%) were very satisfied, 30 (28%) were somewhat satisfied, 7 (7%) were neither satisfied nor dissatisfied, 24 (23%) were somewhat dissatisfied and 6 (6%) were very dissatisfied. Based on the Breast Evaluation Questionnaire, the average improvement from before getting implants was 10% for comfort when not fully dressed, 8% for comfort when fully dressed, and 26% for satisfaction with breast characteristics.

Revision-Reconstruction Patients

For revision-reconstruction patients, 36 (53%) out of the 68 patients enrolled were included in the analysis of circumferential chest size at 6 years. The average increase in circumferential chest size was 0.5 centimeters (0.2 inches).

At 6 years, 37 (54%) out of 68 revision-reconstruction patients enrolled answered the patient satisfaction question. Of these 37 patients, 36 (97%) stated to their surgeon that they would make the same decision to have breast surgery.

With regard to QoL measures at 6 years for revision-reconstruction patients, there was no significant change in the SF-36 or Rosenberg Self Esteem Scale. For the

Body Esteem Scale, there was a significant increase in the chest subscale. Of the 38 revision-reconstruction patients that answered the question "How satisfied with the general appearance of your breasts are you?"; 10 (26%) were very satisfied, 13 (34%) were somewhat satisfied, 2 (5%) were neither satisfied nor dissatisfied, 8 (21%) were somewhat dissatisfied and 5 (13%) were very dissatisfied. Based on the Breast Evaluation Questionnaire, the average improvement from before getting implants was 29% for comfort when not fully dressed, 12% for comfort when fully dressed, and 32% for satisfaction with breast characteristics

3. Subgroup Analyses

a. Rupture Rate and Detection of Rupture

Clinical Study Rupture Rate

In Mentor's MemoryShape™ Core Study, rupture was originally assessed for patients who had scheduled MRIs to screen for silent rupture (i.e., part of the MRI cohort). A total of 419 patients were enrolled in the MRI cohort, including 252 primary augmentation, 56 revision- augmentation, 74 primary reconstruction, and 37 revision-reconstruction patients.

Table 28 shows Kaplan-Meier cumulative incidence rates of occurrence (95% confidence interval) of rupture for all four study cohorts by patient.

Cohort[1]	1 Year		2 Year		4 Year		6 Year	
	n	%	n	%	n	%	n	%
Primary Augmentation, N=252	0	0	0	0	3	1.1 (0.3, 4.2)	4	2.6 (1.0, 6.9)
Revision Augmentation, N=56	0	0	0	0	0	0	1	3.6 (0.5, 22.8)
Primary Reconstruction[2], N=74	1	1.6 (0.2, 11.1)	1	1.6 (0.2, 00.1)	1	1.6 (0.2, 11.1)	1	1.6 (0.2, 11.1)
Revision Reconstruction, N=37	0	0	0	0	0	0	0	0

[1] Rupture was assessed for patients who had MRIs to screen for silent rupture

[2] One primary reconstruction patient from the MRI cohort with a reported rupture of a replacement study device was not included in the rupture analyses because the patient no longer had the original study implant; only original study implants were included in the analyses

Table 28: Kaplan-Meier Cumulative Incidence Rates of Occurrence (95% confidence interval) of Rupture by Cohort for MRI Cohort

Overall, there were 9 suspected or confirmed reports of rupture for 9 of the 955 patients participating in the study, 7 reports among patients in the MRI cohort and 2 reports among patients not in the MRI cohort. One report of a ruptured replacement study implant (primary reconstruction) from the MRI cohort was not included in the rupture analyses because the patient no longer had the original study implant; only original study implants were included in the analyses. Of the 9 suspected or confirmed ruptured implants in the overall study, 1 case was indeterminate for extracapsular silicone by MRI. There were no cases of migrated gel. The rupture rate beyond 6 years in Mentor's MemoryShape™ Core Study continues to be investigated.

In August 2010, a protocol amendment with an FDA mandated change was approved. The amendment specified that "All active patients with study devices will have MRI scans at years 6, 8, and 10". This protocol amendment became active during a time that the 6-year visit windows were coming to a close, and therefore, there were insufficient follow-up data for meaningful Kaplan-Meier analyses of the original "non-MRI" cohort at 6-years. These data will be included in future labeling updates.

Usage of MRI to Detect Rupture

There were 31 explanted devices examined from 19 patients who had undergone an MRI at some point prior to explantation. The average time between MRI and implant explantation was 14 months (range of 1 to 59 months, median of 11 months). For all 31 devices (3 ruptured, 28 intact), the rupture/non-rupture status from all MRIs was confirmed in every case. The results are presented in Table 29.

Implants with history of MRI screening, explantation, and product evaluation	Rupture confirmed on explant	Non-Rupture confirmed on explant
MRI showed rupture	3*	0
MRI showed no rupture	0	28
MRI Sensitivity	100%	
MRI Specificity	100%	
*Of the 9 suspected ruptures or confirmed ruptures in the study, 4 have been explanted. MRI data prior to explant was available for 3 of the 4 explanted devices. In all 3 of these cases, rupture was confirmed by product evaluation after explant (see Figure 3).		

Table 29: MRI Screening Conducted Prior to Explantation

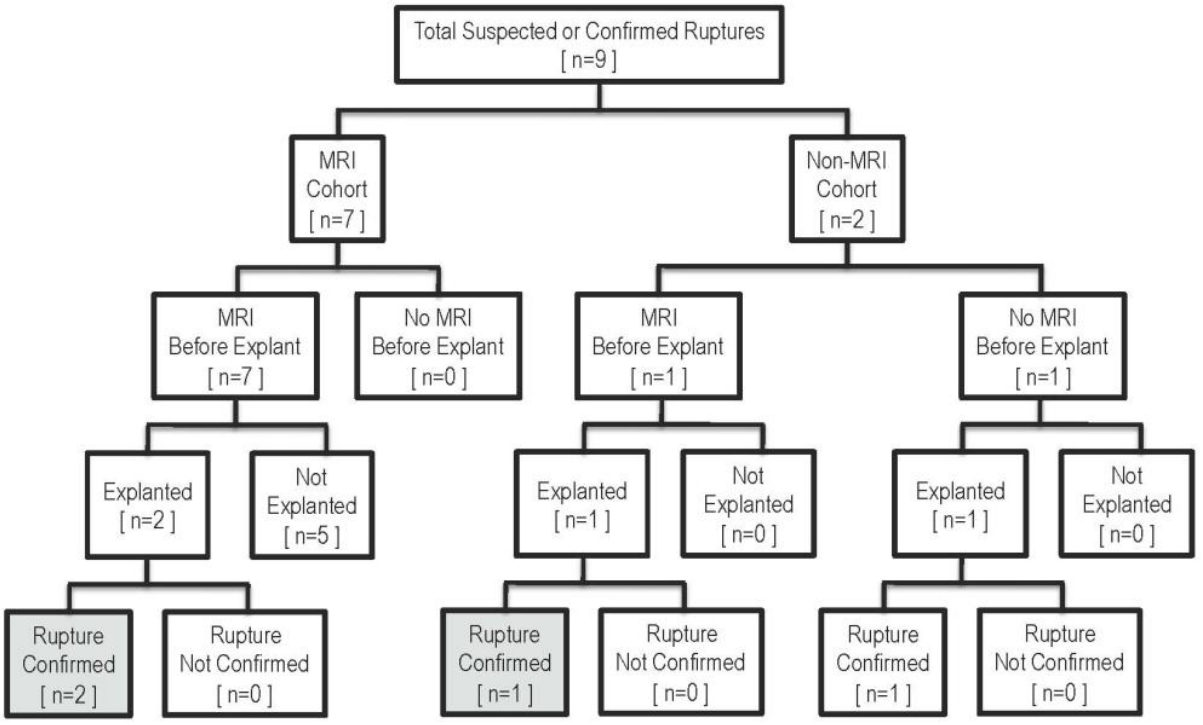

Figure 3: Confirmation of Ruptures by Product Evaluation after Explantation (confirmed ruptures in patients with MRI screening prior to explantation are shown in shaded boxes)

b. Risk Factor Analysis

A risk factor analysis was performed to determine whether there were any risk factors associated with the reported complications. The results of this analysis show that:

- Older age was associated with a decreased risk of any reoperation to the breast or surrounding areas for revision-augmentation patients and revision-reconstruction patients.
- Compared to Caucasian patients, the 'other/missing' race category was associated with a higher risk of explantation regardless of replacement and of any reoperation to the breast or surrounding areas for revision-augmentation patients. The 'other/missing' race category was associated with a lower risk of any complication, excluding rupture for revision-reconstruction patients.
- Compared to the inframammary surgical approach, the 'other/mixed/missing' surgical approaches were associated with an increased risk of any

complication excluding rupture for primary augmentation patients, and mastectomy scar was associated with a decreased risk of any complication excluding rupture for primary reconstruction patients.

- Use of saline and antibiotics in irrigation solutions used in the pocket, as compared to saline only, was associated with a decreased risk of explantation regardless of replacement in primary reconstruction patients. Irrigation solutions used in the pocket was determined to be a statistically significant risk factor for any complication excluding rupture for revision-reconstruction patients, but none of the individual comparisons with the inframammary approach reference category were statistically significant.
- Greater incision size was associated with an increased risk of any complication excluding rupture for revision-reconstruction patients.
- Subglandular surgical placement, as compared to submuscular/subpectoral, was associated with an increased risk of capsular contracture Baker Grade III/IV for primary augmentation patients.
- Investigative site was a statistically significant risk factor for any complication excluding rupture for primary reconstruction patients.
- Catalog number was a statistically significant risk factor for any complication excluding rupture for revision-reconstruction patients.

E. Financial Disclosure

The Financial Disclosure by Clinical Investigators regulation (21 CFR 54) requires applicants who submit a marketing application to include certain information concerning the compensation to, and financial interests and arrangement of, any clinical investigator conducting clinical studies covered by the regulation. The pivotal clinical study included 43 of which none were full-time or part-time employees of the sponsor and one (1) had disclosable financial interests/arrangements as defined in 21 CFR 54.2(a), (b), (c) and (f) and described below:

- Compensation to the investigator for conducting the study where the value could be influenced by the outcome of the study: [0]
- Significant payment of other sorts: [0]
- Proprietary interest in the product tested held by the investigator: [0]
- Significant equity interest held by investigator in sponsor of covered study: [1]

The applicant has adequately disclosed the financial interest/arrangements with clinical investigators. Statistical analyses were conducted by FDA to determine whether the financial interests/arrangements had any impact on the clinical study outcome. The information provided does not raise any questions about the reliability of the data.

XI. SUMMARY OF SUPPLEMENTAL CLINICAL INFORMATION

After enrollment into Mentor's Core study was completed, additional patients were enrolled under a Continued Access Study (CAS) and there was one patient implanted as a "compassionate use" case.

Although one model of the MemoryShape™ Breast Implant was evaluated in the Core study, a larger range of profiles and heights were made available through the CAS and the compassionate use case. Table 30 lists the styles studied in the Core, CAS and the compassionate use case.

	MM	LM+	MM+	MH	TM+
Core	x				
CAS	x	x	x	x	x
Compassionate Use Case		x			

Table 30: Styles Evaluated in the Clinical Studies

Continued Access Study (CAS)

The purpose of the CAS is to provide participating surgeons with additional experience with the Mentor MemoryShape™ device. The CAS approval was limited to the 43 investigators and 78 sites that were involved in the Core study. CAS enrollment was limited to 60 patients per month for a period of 6 months. Each 6 month time frame is renewable. Patient enrollment began in August 2004 and there were a total of 3,562 subjects enrolled over 103 months at the time of the CAS database closure in January 2013. This includes a total of 6,886 study implants, of which 3,929 were style MM. The CAS continues to enroll patients; however enrollment into the CAS ceased on the date of FDA Notice of Approval. The CAS patients are enrolled under a protocol that differs from the Core study in that:

1. Data for effectiveness, rheumatic symptoms were not collected.
2. There is no requirement to participate in a MRI cohort, and as such, related enrollment criteria was modified
3. The informed consent document was modified according to the protocol changes

Table 31 shows the Kaplan-Meier cumulative incidence rates of complications through 6 years noted in the CAS.

Complications Through 6 Years[1]	Primary Augmentation[2] N=2337	Revision-Augmentation[3] N=543	Primary Reconstruction[4] N=431	Revision-Reconstruction[5] N=252
Overall Complications and Reoperations				
Any Complication	16.8%	20.4%	28.1%	30.3%
Any Complication Excluding Cosmetic	12.1%	15.7%	25.2%	29.0%
Any Complication or Reoperation	19.3%	23.9%	36.6%	40.3%
Any Cosmetic Complication[6]	6.4%	6.3%	6.3%	3.2%
Any Reoperation	10.5%	19.9%	26.5%	30.9%
Implant Removal with or without Replacement	5.0%	10.6%	16.1%	19.7%
Individual complications				
3rd Degree Sunburn	0%	0%	0%	1.0%
Asymmetry	0.1%	0.2%	2.5%	0.9%
Atrophy	0%	0%	0.3%	0%
Baker II Capsular Contracture w/Surgical Intervention	0.3%	0.2%	1.5%	2.2%
Baker III Capsular Contracture	0.9%	0.3%	2.7%	7.6%
Baker IV Capsular Contracture	0.2%	0.3%	0.3%	1.0%
Baker III, IV Capsular Contracture	1.0%	0.5%	3.0%	8.7%
Breast Sensation Changes	0.4%	0.3%	0%	0%
Breast pain	0.2%	1.1%	0.2%	0.7%
Bruising	0.2%	0%	0%	0%
CIPD	0.2%	0%	0%	0%
Contact Dermatitis	0.1%	0%	0%	0%
Contour Irregularities	0.1%	0%	1.8%	4.7%
Contralateral Explant Due To Baker III	0%	0%	0%	1.5%
Contralateral Explant Due To Wound Dehiscence	0%	0%	0.2%	0%
Death[7]	0.2%	0.9%	2.4%	1.7%
Delayed Wound Healing	0.1%	0.2%	0.5%	0.4%
Double Bubble	0.1%	0%	0%	0%
Drainage	<0.05%	0.2%	0%	0%
Ehlers-Danlos Syndrome	0%	0%	1.9%	0%
Erythema (redness)	0.1%	0.2%	0.3%	0%
Excess Skin/Tissue	0.1%	0%	0.3%	0%
External Injury to Breast	<0.05%	0%	0%	0%
Extrusion	<0.05%	0.9%	0.8%	0%
Hematoma	0.6%	1.7%	0.5%	0%
Hypertrophic Scarring	1.2%	1.4%	0.9%	0.6%
Immobile Implant	0.1%	0%	0%	0%
Implant Rotation	0.5%	1.5%	1.8%	1.8%
Indeterminate MRI	0%	0%	0%	2.3%
Infection	0.7%	1.2%	1.6%	0.9%
Irritation/Inflammation	0.3%	0%	0%	0.9%
Lack of Projection	0%	0.2%	0%	2.4%
Lactation Difficulties	1.0%	0%	0%	0%
Loss of Definition Of Inframammary Fold	0.1%	0%	0%	0%

Complications Through 6 Years[1]	Primary Augmentation[2] N=2337	Revision-Augmentation[3] N=543	Primary Reconstruction[4] N=431	Revision-Reconstruction[5] N=252
Low Breast Volume	0%	0.2%	0%	0%
Lower Pole Fullness	0%	0%	2.0%	0%
Lyme Disease	0.1%	0%	0%	0%
Lymphadenopathy	0.1%	0%	0%	0%
Lymphoma	0%	0.2%	0%	0%
Mass/Cyst	2.2%	2.9%	1.9%	4.2%
Metastatic Cancer	0%	0%	0.7%	0.7%
Miscarriage	0.3%	0%	0%	0%
Monder's Disease	0.1%	0%	0%	0%
Multiple Sclerosis	0.1%	0%	0%	0%
Necrosis	0.1%	0%	0.2%	0%
Nerve Pain	0.1%	0%	0%	0%
Neuropathic Pain	0.1%	0%	0%	0%
New Diagnosis of Breast Cancer	0.7%	0.3%	0%	0%
New Diagnosis of Rheumatic Disease	0.4%	0.3%	0%	0.8%
Nipple Complications	0.1%	0.3%	0%	0%
Nipple Sensation Changes	0.1%	0%	0%	0%
Other: Missing	0.2%	0%	0%	0.7%
Palpability-Implant	0.2%	0%	1.1%	0%
Patient Dissatisfied with Aesthetic Appearance of Breast	0.7%	0.6%	0.5%	0%
Patient Dissatisfied with Feel of Breast	0.2%	0%	0%	0%
Patient Dissatisfaction	0.1%	0%	0%	0%
Patient Dissatisfied with Breast Size	0.1%	0%	0%	0%
Patient Requested Removal	0.1%	0%	0.8%	0%
Position Dissatisfaction	0.5%	0.7%	0.6%	2.6%
Ptosis	3.7%	1.1%	1.2%	0%
Recurrent Breast Cancer	0%	0%	0%	2.0%
Rib Pain	0%	0.4%	0%	0%
Rupture	0%	0%	0.7%	0%
Scarring	0.6%	0.2%	0.7%	0.7%
Sensation Changes	0.2%	0%	0%	0%
Seroma	0.3%	2.0%	1.3%	0.9%
Size Change-Patient Request	1.3%	1.7%	1.3%	1.8%
Size Change-Physician Assessment Only	0.1%	0.2%	0.3%	0%
Skin Complication	0.3%	0%	0.3%	0%
Skin Lesion	0.2%	0%	0%	0%
Small 2mm Opening Down to the Implant - Right Breast	0%	0%	0.2%	0%
Sternal Pain	<0.05%	0%	0%	0%
Suture Complication	0.1%	0%	0%	0%
Swelling (Excessive)	0.1%	0.7%	0.5%	0%
Symmastia	0.1%	0%	0%	0%
Tightness of Skin Over Implant	0%	0%	0%	0.5%
Wound Dehiscence	0.1%	0.8%	1.3%	0%

Complications Through 6 Years[1]	Primary Augmentation[2] N=2337	Revision-Augmentation[3] N=543	Primary Reconstruction[4] N=431	Revision-Reconstruction[5] N=252
Wrinkling	0.4%	2.1%	0.5%	0%

1Excludes mild occurrences of the following: asymmetry, breast pain, breast sensation changes, calcification, delayed wound healing, nipple sensation changes, position dissatisfaction, nipple complications, wrinkling, and palpability-implant.
2 297 primary augmentation patients experienced at least one complication or reoperation
3 99 revision augmentation patients experienced at least one complication or reoperation
4 102 primary reconstruction patients experienced at least one complication or reoperation
5 57 revision reconstruction patients experienced at least one complication or reoperation
6 Cosmetic complications include asymmetry, hypertrophic scarring, ptosis, size-change-patient request, size change-physician assessment only, and wrinkling.
7 All causes of death were reported by the Investigator to be unrelated to study procedure or device.

Table 31: KM Risk Rates Through 6 Years for the Continued Access Study

Compassionate Use Case

In addition, one patient had been implanted with a MemoryShape™ Breast Implant as a "compassionate use" case. The purpose of this compassionate use option was to allow a non-Core study physician access to the device, as they had a patient that required an anatomically shaped implant for breast reconstruction. Approval from the FDA to treat 1 patient outside of the study protocol was granted in July 2010. Using the clinical study protocol as a guide, the attending physician devised an appropriate monitoring schedule. There have been no reports of adverse events for this patient.

XII. PANEL MEETING RECOMMENDATION AND FDA'S POST-PANEL ACTION

In accordance with the provisions of section 515(c)(2) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the General and Plastic Surgery Advisory Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

XIII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Effectiveness Conclusions

The effectiveness outcomes demonstrate that the majority of subjects report favorable satisfaction and QoL results. In addition, the vast majority of patients who underwent a measurement of breast cup size change (primary augmentation cohort only), report an increase in bra cup-size by at least one cup size.

B. Safety Conclusions

The risks of the device are based on nonclinical laboratory data as well as data collected in a clinical study conducted to support PMA approval as described above.

The most commonly experienced complication in all cohorts was reoperation. The incidence rates of reoperation 6-years were 18% for primary augmentation 24% for revision-augmentation, 45% for primary reconstruction, and 45% for revision-reconstruction. The safety assessment of MemoryShape™ Breast Implants reveals clinically acceptable rates for complications associated with silicone gel breast implants, and, in general, demonstrate that the risk of complications associated with Mentor's MemoryShape™ Breast Implants is relatively low.

C. Benefit-Risk Conclusions

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

Additional factors to be considered in determining probable risks and benefits for the Mentor MemoryShape™ device included: the active and deliberate search/documentation of adverse events in the pivotal study, single arm pivotal study design, lacking individual patient success criteria, good patient follow-up through 6 years, the availability of alternative treatments, patient-centric assessments, and risk mitigation with device use by trained surgeons in patients with informed consent.

In conclusion, given the available information above, the data support that the probable benefits outweigh the probable risks for females for Mentor MemoryShape™ Breast Implants for the following procedures:

- Breast augmentation for women at least 22 years old. Breast augmentation includes primary breast augmentation to increase the breast size, as well as revision surgery to correct or improve the results of a primary breast augmentation surgery.

- Breast reconstruction. Breast reconstruction includes primary reconstruction to replace breast tissue that has been removed due to cancer or trauma or that has failed to develop properly due to a severe breast abnormality. Breast reconstruction also includes revision surgery to correct or improve the result of a primary breast reconstruction surgery.

D. Overall Conclusions

The data in this application support the reasonable assurance of safety and effectiveness of this device when used in accordance with the indications for use. The benefits and risks of breast implants are sufficiently well understood for women to make informed decisions about their use. The 6-year clinical results demonstrate that MemoryShape™ Breast Implants are reasonably safe and effective for use in primary augmentation, revision-augmentation, primary reconstruction, and revision-reconstruction of the breast.

XIV. CDRH DECISION

CDRH issued an approval order on June 14, 2013. The final conditions of approval cited in the approval order are described below.

1. Post-Approval PMA Cohort Study (PACS)

Per Post-Approval PMA Cohort Study protocol version dated January 22, 2010, this study will consist of the continued follow-up of premarket cohorts. Study participants will be followed annually for 10 years in order to assess the long-term clinical performance of their device. The Post-Approval PMA Cohorts Study (PACS) will include a total of 955 subjects. The PACS data are to be collected via annual physician follow-up evaluations and all patients in the study will have MRI at years 8 and 10. All safety and effectiveness endpoints evaluated at premarket will continue to be studied long-term. The safety endpoints include local complications, implant rupture, rheumatologic diseases and rheumatologic signs and symptoms. Descriptive statistics will be provided for all endpoints. The association between the studied endpoints and Mentor's approved device will be assessed as per protocol version dated January 22, 2010. Additional analyses will be performed as per agreement reached on September 11, 2012 (e-mail). Mentor is also required to conduct Device Explant Analyses for all devices retrieved from women enrolled in the PACS as outlined in the protocol version dated August 12, 2012. Mentor must report results of these explant analyses in the post-approval study Annual Report.

Mentor must also update their patient and physician labeling to reflect 10-year PACS study findings on the safety and effectiveness of the device, as soon as these data are available, as well as any other time point deemed necessary by FDA if significantly new information from this study becomes available. On an annual basis, Mentor must submit a PACS progress report to FDA that includes: (1) the follow-up status of study subjects; and (2) a summary of findings for all study endpoints.

2. Post-approval Continued Access Study (PACAS)

Per Post-approval Continued Access Study protocol version dated April 18, 2013 (e-mail), the Post-Approval Continued Access Study (PACAS) will consist of the continued follow-up, for 5-years post-implantation, of approximately 350 subjects who were previously enrolled before the date of approval in the Continued Access Study and implanted with MemoryShape™ Medium Height Moderate Profile (CPG Style 321) Breast Implants. All safety endpoints evaluated premarket will continue to be studied through 5-years of follow-up. Descriptive statistics will be provided. Mentor is also required to conduct Device Explant Analyses for all devices retrieved from women enrolled in the PACAS as outlined in the protocol version dated August 12, 2012. Mentor must report results of these explant analyses in the post-approval study Annual Report.

On an annual basis and until the completion of 5year follow-up for all PACAS subjects, Mentor must submit a PAS progress report to the FDA that includes: patient compliance, a summary of findings for all study endpoints, and results of the device explant analyses for devices explanted within this study.

3. MemoryShape™ Post-Approval Study (MemoryShape™ PAS)

Per MemoryShape™ Post-approval Study protocol version October 25, 2012 (e-mail), this study is a newly enrolled cohort study in the US. The purpose of this study is to evaluate the long-term clinical performance of MemoryShape™ Breast Implants under general conditions of use in the postmarket environment. The study will enroll 2,518 women receiving MemoryShape™ Breast Implants and 300 women undergoing other aesthetic surgery as the comparison group. Study subjects will be followed annually for 10 years. Data will be collected on the following safety endpoints: connective tissue diseases (CTDs), rheumatologic and neurologic signs and symptoms, cancer (lung and breast, including the potential of breast implant interference with mammography and delay of breast cancer detection), suicide/attempted suicide, local complications (including infection, rupture; including rupture rate following mammography), reoperation and implant removal, reproductive complications in women who attempt to have children, lactation complications, and congenital deformities. The effectiveness will be assessed by participants' responses to questions addressing their perceived quality of life and satisfaction with their breast implants.

Data are to be collected via annual patient questionnaires. There will also be physician evaluations at years 1, 5, and 10. Descriptive statistics will be provided for the studied endpoints. In addition, the association between the studied endpoints and Mentor's approved device will be assessed as per protocol version dated October 25, 2012. Mentor is also required to conduct Device Explant Analyses for all devices retrieved from women enrolled

in the MemoryShape™ PAS per protocol version dated August 12, 2012. Mentor must report results of these explant analyses in the post-approval study Annual Report.
Mentor also agrees to participate as a stakeholder in developing the National Breast Implants Registry and to contribute data from their MemoryShape™ US Post-Approval Study to the Registry upon its implementation. Please be advised that because the establishment of the National Breast Implants Registry is currently in progress, this condition of approval will be labeled as "Study Pending" upon further notification from the FDA. Under this agreement, Mentor must submit interim reports every 6 months that include: (1) activities that they undertake for the development of the National Breast Implant Registry; (2) US sales data for the MemoryShape™ breast implants; and (3) US implant data for the MemoryShape™ breast implants.

Otherwise, Mentor's reporting requirements for the MemoryShape™ US-PAS are as follows:

On a quarterly basis, they must submit a report to FDA that includes: (1) the number enrolled by subjects receiving studied device versus enrolled in comparison group; (2) the number enrolled by indication (primary augmentation, revision-augmentation, primary reconstruction, revision-reconstruction) for subjects receiving studied device; (3) the number enrolled by race/ethnicity; (4) the enrollment rates versus the stated goals; (5) the reason why eligible patients were not enrolled into the study; and (6) the follow-up rates versus the stated goals. FDA will inform Mentor when quarterly reports are no longer necessary.

In addition, every 6 months for the first 2 years and then annually, thereafter, Mentor is to submit a progress report that includes: (1) the status of patient enrollment as it compares to the stated goals; (2) the status of the race/ethnicity distribution as it compares to the stated goals; (3) detailed patient and device accounting; (4) the reasons why eligible patients were not enrolled into the study; (5) the follow-up rates versus the stated goals; and (6) a summary of findings for all study endpoints.
Mentor must update their patient and physician labeling to reflect 5 and 10-year MemoryShape™ PAS study findings, as soon as these data are available, as well as any other time point deemed necessary by FDA if significantly new information from this study becomes available.

4. Breast Implant Case-Control Studies To Address Rare Disease Outcomes

In order to evaluate the rare endpoints, FDA approves Mentor's proposal to conduct case-controlled studies using data that is already collected in countries where the device has been on the market for years. Per Breast Implant Case-Control Studies To Address Rare Disease Outcomes protocols version dated September 11, 2012, the purpose of Breast Implant Case-Control Studies To Address Rare Disease Outcomes are to evaluate the association between

MemoryShape™ Silicone-Filled Breast Implants and five rare disease outcomes (rare connective tissue diseases, rare neurological diseases, brain cancer, cervical/vulvar cancer and lymphoma). These studies will be conducted in Denmark, Germany and the United Kingdom and will enroll a total of 5,750 cases and 5,000 controls. For each of the five rare disease outcomes, 1,150 cases will be enrolled and compared to the controls on the history of the implantation of Mentor silicone gel-filled breast implants.

On a quarterly basis, Mentor must submit a report to FDA that includes: (1) the number enrolled by cases and controls; (2) the enrollment rate versus the stated goal. FDA will inform Mentor when quarterly reports are no longer necessary. In addition, within 3 months of the completion of subject enrollment and data collection, Mentor must submit a final Breast Implant Case-Control Studies To Address Rare Disease Outcomes study report that includes the results and conclusions of these studies.

5. Focus Group Study

Per Focus Group Study protocol version dated September 11, 2012, the purpose of the Focus Group Study is to evaluate the effectiveness of the informed decision material intended to educate potential breast implant surgery patients about the risks, complications, and benefits associated with breast implants and breast implant surgery. This will involve an independent group obtaining responses from patients on the content of the approved labeling. Upon completion of the focus group study, Mentor must submit a Final Report of the focus group study findings and suggested revision of patient and physician labeling based on those findings.

6. Device Explant Analysis

In addition to the studies listed above, Mentor must conduct non-PAS Device Explant Analyses for all MemoryShape™ Breast Implants that are retrieved in the commercial setting outside the post-approval studies, as per explant analysis protocol version dated August 12, 2012. On an annual basis, Mentor must report the results of these Device Explant Analyses in the PMA Annual Reports.

The applicant's manufacturing facility was inspected and found to be in compliance with the device Quality System (QS) regulation (21 CFR 820).

XV. APPROVAL SPECIFICATIONS

Directions for use: See device labeling.

Hazards to Health from Use of the Device: See Indications, Contraindications, Warnings, Precautions, and Adverse Events in the device labeling.

Post-approval Requirements and Restrictions: See approval order.

XVI. REFERENCES

[i] Raposo do Amaral, C.M.60 et al. (1993). Aesthetic Plastic Surgery. 17, 335-338.

[ii] Swanson, A.B. et al. (1985). "Host Reaction to Silicone Implants: A Long-Term Clinical and Histopathological Study", Corrosion and Degradation of Implant Materials: Second Symposium, ASTM STP 859, A.C. Fraker and C.D. Griffin, Eds., American Society for Testing and Materials, Philadelphia, 267-277.

[iii] Kala, S.V., et al. (1998). Low Molecular Weight Silicones are Widely Distributed after a Single Subcutaneous Injection in Mice. A. J. Path. 152, 645-649.

[iv] Plotzke K.P., et al. (2000). Disposition of radioactivity in Fischer 344 rats after single and multiple inhalation exposure to [^{14}C]octamethylcyclotetrasiloxane ([^{14}C]D_4). Drug Metab. Dispos. 28(2):192-204

[v] Andersen M.E., et al. (2001). Physiological modeling reveals novel pharmacokinetic behavior for inhaled octamethylcyclotetrasiloxane in rats. Toxicol. Sci. 60(2):214-231

[vi] Meeks, R.G. (2002). Bioavailability of D4 after inhalation and implantation exposure to silicones. Environ. Health Perspect. 110(8):A442-A443; Andersen M.E., et al. (2002). Further comments on the bioavailability of D4. Environs Health. Perspect. 110(8):A444-A445; Clewell, H. (2003). Critical Evaluation of the Pharmacokinetic Model for D4. Developed by Luu and Hutter. ENVIRON International Corporation. Ruston, LA 71270. 8 pp. (Unpublished).

[vii] Flassbeck, D.B., et al. 2003. Determination of siloxanes, silicon, and platinum in tissues of women with silicone gel-filled implants. Anal. Bioanal. Chem. 375(3):356-62 (for example, data from Patients B & C).

[viii] Bondurant, S., V.L. Ernster and R. Herdman, Eds. 2000. Safety of silicone breast implants. Committee on the Safety of Silicone Breast Implants, Division of Health Promotion and Disease Prevention, Institute of Medicine. Washington, D.C.: National Academy Press.

[ix] Katzin, W.E., et al. 2005. Pathology of lymph nodes from patients with breast implants: a histologic and spectroscopic evaluation. Am. J. Surg. Pathol. 29(4):506-11.

[x] Stein, J., et al. 1999. In situ determination of the active catalyst in hydrosilylation reactions using highly reactive Pt(0) catalyst precursors. J. Am. Chem. Soc. 121(15):3693-703.

[xi] Chandra, G., et al. 1987. A convenient and novel route to bis(alkyne)platinum(0) and other platinum(0) complexes from Speier's hydrosilylation catalyst. Organometallics. 6:191-2.

[xii] Lappert, M.F. and Scott, F.P.A. 1995. The reaction pathway from Speier's to Karstedt's hydrosilylation catalyst. J. Organomet. Chem. 492(2):C11-C13.

[xiii] Lewis, L.N., et al. 1995. Mechanism of formation of platinum(0) complexes containing silicon-vinyl ligands. Organometallics. 14:2202-13.