

Informal Core Study Emails

Topic	Table(s)/Attachment	Email Date
Patient Deaths- clarification of cumulative numbers	Tables 19 and 20 discussed	07/11/03
Recalculated confidence intervals for 3 -year Recon using Peto's formula	Tables 21, 25, 29A, 29B, 33, 37, 41, 45, 49A, 49B, 53, 57, 61, 65, 69, 73A, 73B, 77, 81, 85, 89A, 89B, 93A, 93B, 97, 101, 105A, 105B, 109A, 109B, 113, 117A, 117B, 121A, 121B, 125A, 125B, 129, 133, 137A, 137B, 141A, 141B, 145A, 145B, 149, 153A, 153B, 160, 163, 171, 172, 173, 178, 179, 180 (Core Recon Risk of First Occurrence of Complications)	07/23/03
Correction to Table 168: Primary Reason For Reoperation and Primary Procedure Performed	Table 168	07/28/03
Updated Suspected Rupture Tables Response to Deficiency 3 Question	Core Clinical Study Rupture Tables (not numbered)	07/29/03
Confirmed Non-Rupture Reports, Corrected Core Clinical Study Rupture Tables	Multiple MRI, diagnostic and Op notes related to Confirmed Core Non-Ruptures; Corrected Core Clinical Study Rupture Tables	08/01/03
Ruptures by Implant Style	Attached Tables (not numbered): Core Study Confirmed/Unconfirmed Ruptures by Implant Style	08/06/03
Correction to Augmentation Risk of First Occurrence Tables	Attached: Corrected Tables 171, 173, 173A, 174, 175	08/08/03
3-Year Complication Rates for Augmentation Patients in Core Study and 1995 Saline Study	Revised Appendix G	08/10/03
MRI : Patient compliance and risk analysis	Attached: Tables 2A (Serial MRI Patient Compliance) and 7 (Risk of First Occurrence of Silent Rupture)	08/20/03
KM Silent Rupture Rates by implant	Tables 7A, 7B, 7C, 7D, and Table 1: Risk of First Occurrence of Silent Rupture	08/30/03
MRI screening compliance	Table 2B Number of Patients/ Implants with MRIs	09/01/03
Analysis of Activities and Lifestyle data	Connective Tissue Disease (CTD) Signs/Symptoms	09/01/03

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Table 25: Risk of First Occurrence of Breast Pain (>= Moderate Severity)

Time.	By Patient				By Implant			
	Number Affected	Number Remaining	Cumulative Risk	% (95% CI)	Number Affected	Number Remaining	Cumulative Risk	% (95% CI)
	n	n	% (95% CI)		n	n	% (95% CI)	
4 Weeks	3	216	1.4% (0.0%, 2.9%)		4	354	1.1% (0.0%, 2.2%)	
6 Months	5	202	2.3% (0.2%, 4.3%)		6	330	1.7% (0.3%, 3.0%)	
1 Year	7	191	3.3% (0.8%, 5.7%)		9	311	2.6% (0.8%, 4.3%)	
2 Years	7	178	3.3% (0.7%, 5.8%)		9	291	2.6% (0.8%, 4.4%)	
3 Years	10	90	6.0% (1.2%, 10.8%)		12	142	4.3% (1.0%, 7.6%)	

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Table 29A: Risk of First Occurrence of Bruising (>= Moderate Severity)

Time	By Patient				By Implant			
	Number Affected	Number Remaining	Cumulative Risk	% (95% CI)	Number Affected	Number Remaining	Cumulative Risk	% (95% CI)
	n	n			n	n		
4 weeks	3	216	1.4%	(0.0%, 2.9%)	4	354	1.1%	(0.0%, 2.2%)
6 Months	3	203	1.4%	(0.0%, 2.9%)	4	330	1.1%	(0.0%, 2.2%)
1 Year	3	194	1.4%	(0.0%, 3.0%)	4	314	1.1%	(0.0%, 2.3%)
2 Years	3	180	1.4%	(0.0%, 3.0%)	4	292	1.1%	(0.0%, 2.3%)
3 Years	3	90	1.4%	(0.0%, 3.7%)	4	140	1.1%	(0.0%, 2.8%)

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Table 29B: Risk of First Occurrence of Bruising (All Severity Levels)

Time	By Patient				By Implant			
	Number Affected	Number Remaining	Cumulative Risk	% (95% CI)	Number Affected	Number Remaining	Cumulative Risk	% (95% CI)
	n	n	%	(95% CI)	n	n	%	(95% CI)
4 weeks	6	213	2.7%	(0.6%, 4.9%)	9	349	2.5%	(0.9%, 4.1%)
6 Months	9	197	4.1%	(1.4%, 6.8%)	12	322	3.4%	(1.4%, 5.3%)
1 Year	9	188	4.1%	(1.3%, 6.9%)	12	306	3.4%	(1.4%, 5.3%)
2 Years	9	174	4.1%	(1.2%, 7.0%)	12	284	3.4%	(1.3%, 5.4%)
3 Years	9	88	4.1%	(0.0%, 8.2%)	12	137	3.4%	(0.4%, 6.3%)

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Table 33: Risk of First Occurrence of Capsule Calcification (>= Moderate severity)

Time	By Patient				By Implant			
	Number Affected	Number Remaining	Cumulative Risk	% (95% CI)	Number Affected	Number Remaining	Cumulative Risk	% (95% CI)
	n	n	%	(95% CI)	n	n	%	(95% CI)
4 Weeks	0	219	0.0%	--	0	358	0.0%	--
6 Months	0	205	0.0%	--	0	333	0.0%	--
1 Year	0	196	0.0%	--	0	317	0.0%	--
2 Years	0	182	0.0%	--	0	295	0.0%	--
3 Years	0	92	0.0%	--	0	143	0.0%	--

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Table 37: Risk of First Occurrence of Capsular Contracture (>= Moderate Severity)

Time	By Patient				By Implant			
	Number Affected	Number Remaining	Cumulative Risk		Number Affected	Number Remaining	Cumulative Risk	
	n	n	% (95% CI)		n	n	% (95% CI)	
4 Weeks	6	213	2.7% (0.6%, 4.9%)		7	351	2.0% (0.5%, 3.4%)	
6 Months	15	193	7.0% (3.5%,10.4%)		17	319	4.9% (2.6%, 7.1%)	
1 Year	22	179	10.4% (6.2%,14.6%)		25	297	7.3% (4.4%,10.1%)	
2 Years	27	164	12.9% (8.1%,17.7%)		30	275	8.9% (5.6%,12.1%)	
3 Years	31	79	16.1% (8.7%,23.6%)		35	128	11.2% (6.1%,16.3%)	

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Table 41: Risk of First Occurrence of Delayed Wound Healing (>= Moderate severity)

Time	By Patient				By Implant			
	Number Affected	Number Remaining	Cumulative Risk	% (95% CI)	Number Affected	Number Remaining	Cumulative Risk	% (95% CI)
	n	n	%	(95% CI)	n	n	%	(95% CI)
4 weeks	2	217	0.9%	(0.0%, 2.2%)	2	356	0.6%	(0.0%, 1.3%)
6 Months	5	201	2.3%	(0.3%, 4.4%)	5	329	1.4%	(0.2%, 2.7%)
1 Year	5	192	2.3%	(0.2%, 4.4%)	5	313	1.4%	(0.1%, 2.7%)
2 Years	5	178	2.3%	(0.1%, 4.5%)	5	291	1.4%	(0.1%, 2.8%)
3 Years	5	91	2.3%	(0.0%, 5.4%)	5	142	1.4%	(0.0%, 3.4%)

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Table 45: Risk of First Occurrence of Fluid Accumulation

N/A: FLUID ACCUMULATION HAS BEEN COMBINED WITH SEROMA

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Table 49A: Risk of First Occurrence of Hematoma (>= Moderate Severity)

Time	By Patient				By Implant			
	Number Affected	Number Remaining	Cumulative Risk	% (95% CI)	Number Affected	Number Remaining	Cumulative Risk	% (95% CI)
	n	n	%	(95% CI)	n	n	%	(95% CI)
4 weeks	1	218	0.5%	(0.0%, 1.3%)	1	357	0.3%	(0.0%, 0.8%)
6 Months	1	204	0.5%	(0.0%, 1.4%)	1	332	0.3%	(0.0%, 0.8%)
1 Year	1	195	0.5%	(0.0%, 1.4%)	1	316	0.3%	(0.0%, 0.9%)
2 Years	1	181	0.5%	(0.0%, 1.4%)	1	294	0.3%	(0.0%, 0.9%)
3 Years	1	91	0.5%	(0.0%, 1.8%)	1	142	0.3%	(0.0%, 1.1%)

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Table 49B: Risk of First Occurrence of Hematoma (All severity Levels)

Time	By Patient				By Implant			
	Number Affected	Number Remaining	Cumulative Risk	% (95% CI)	Number Affected	Number Remaining	Cumulative Risk	% (95% CI)
	n	n	% (95% CI)	% (95% CI)	n	n	% (95% CI)	% (95% CI)
4 Weeks	2	217	0.9% (0.0%, 2.2%)	0.6% (0.0%, 1.3%)	2	356	0.6% (0.0%, 1.3%)	0.6% (0.0%, 1.3%)
6 Months	2	203	0.9% (0.0%, 2.2%)	0.6% (0.0%, 1.3%)	2	331	0.6% (0.0%, 1.3%)	0.6% (0.0%, 1.3%)
1 Year	2	194	0.9% (0.0%, 2.2%)	0.6% (0.0%, 1.4%)	2	315	0.6% (0.0%, 1.4%)	0.6% (0.0%, 1.4%)
2 Years	2	180	0.9% (0.0%, 2.3%)	0.6% (0.0%, 1.4%)	2	293	0.6% (0.0%, 1.4%)	0.6% (0.0%, 1.4%)
3 Years	2	91	0.9% (0.0%, 2.9%)	0.6% (0.0%, 1.8%)	2	142	0.6% (0.0%, 1.8%)	0.6% (0.0%, 1.8%)

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Table 53: Risk of First Occurrence of Hypertrophic Scarring

N/A: HYPERTROPHIC SCARRING HAS BEEN COMBINED WITH OTHER ABNORMAL SCARRING

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Table 57: Risk of First Occurrence of Implant Extrusion (All severity Levels)

Time	By Patient				By Implant			
	Number Affected	Number Remaining	Cumulative Risk		Number Affected	Number Remaining	Cumulative Risk	
	n	n	% (95% CI)		n	n	% (95% CI)	
4 weeks	0	219	0.0%	--	0	358	0.0%	--
6 Months	1	204	0.5% (0.0%, 1.4%)		1	333	0.3% (0.0%, 0.8%)	
1 Year	1	195	0.5% (0.0%, 1.4%)		1	317	0.3% (0.0%, 0.9%)	
2 Years	1	181	0.5% (0.0%, 1.4%)		1	295	0.3% (0.0%, 0.9%)	
3 Years	1	92	0.5% (0.0%, 1.8%)		1	143	0.3% (0.0%, 1.1%)	

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Table 61: Risk of First Occurrence of Implant Malposition (>= Moderate Severity)

Time	By Patient				By Implant			
	Number Affected	Number Remaining	Cumulative Risk		Number Affected	Number Remaining	Cumulative Risk	
	n	n	% (95% CI)		n	n	% (95% CI)	
4 weeks	3	216	1.4% (0.0%, 2.9%)		3	355	0.8% (0.0%, 1.8%)	
6 Months	9	197	4.2% (1.4%, 6.9%)		13	321	3.7% (1.7%, 5.8%)	
1 Year	9	190	4.2% (1.4%, 7.0%)		13	308	3.7% (1.7%, 5.8%)	
2 Years	11	176	5.2% (2.0%, 8.4%)		15	286	4.4% (2.1%, 6.7%)	
3 Years	11	91	5.2% (0.8%, 9.7%)		15	141	4.4% (1.1%, 7.7%)	

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Table 65: Risk of First Occurrence of Implant Palpability

N/A: IMPLANT PALPABILITY HAS BEEN COMBINED WITH IMPLANT VISIBILITY

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Table 69: Risk of First Occurrence of Implant Palpability / Visibility (>= Moderate Severity)

Time	By Patient				By Implant			
	Number Affected	Number Remaining	Cumulative Risk	% (95% CI)	Number Affected	Number Remaining	Cumulative Risk	% (95% CI)
	n	n	% (95% CI)	% (95% CI)	n	n	% (95% CI)	% (95% CI)
4 weeks	1	218	0.5% (0.0%, 1.3%)	0.3%	1	357	0.3% (0.0%, 0.8%)	0.3%
6 Months	1	205	0.5% (0.0%, 1.4%)	0.3%	1	333	0.3% (0.0%, 0.8%)	0.3%
1 Year	1	196	0.5% (0.0%, 1.4%)	0.3%	1	317	0.3% (0.0%, 0.9%)	0.3%
2 Years	1	182	0.5% (0.0%, 1.4%)	0.3%	1	295	0.3% (0.0%, 0.9%)	0.3%
3 Years	1	92	0.5% (0.0%, 1.8%)	0.3%	1	143	0.3% (0.0%, 1.1%)	0.3%

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Table 73A: Risk of First Occurrence of Infection (>= Moderate Severity)

Time	By Patient				By Implant			
	Number Affected	Number Remaining	Cumulative Risk	% (95% CI)	Number Affected	Number Remaining	Cumulative Risk	% (95% CI)
	n	n	%	(95% CI)	n	n	%	(95% CI)
4 weeks	3	216	1.4%	(0.0%, 2.9%)	4	354	1.1%	(0.0%, 2.2%)
6 Months	5	200	2.3%	(0.3%, 4.4%)	6	327	1.7%	(0.3%, 3.1%)
1 Year	5	191	2.3%	(0.2%, 4.4%)	6	311	1.7%	(0.3%, 3.1%)
2 Years	5	177	2.3%	(0.1%, 4.5%)	6	289	1.7%	(0.2%, 3.2%)
3 Years	5	91	2.3%	(0.0%, 5.4%)	6	142	1.7%	(0.0%, 3.8%)

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Table 73B: Risk of First Occurrence of Infection (All severity Levels)

Time	By Patient				By Implant				
	Number Affected	Number Remaining	Cumulative Risk	Number Affected	Number Remaining	Cumulative Risk	Number Affected	Number Remaining	Cumulative Risk
	n	n	% (95% CI)	n	n	% (95% CI)	n	n	% (95% CI)
4 Weeks	3	216	1.4% (0.0%, 2.9%)	4	354	1.1% (0.0%, 2.2%)	4	354	1.1% (0.0%, 2.2%)
6 Months	5	200	2.3% (0.3%, 4.4%)	6	327	1.7% (0.3%, 3.1%)	6	327	1.7% (0.3%, 3.1%)
1 Year	5	191	2.3% (0.2%, 4.4%)	6	311	1.7% (0.3%, 3.1%)	6	311	1.7% (0.3%, 3.1%)
2 Years	5	177	2.3% (0.1%, 4.5%)	6	289	1.7% (0.2%, 3.2%)	6	289	1.7% (0.2%, 3.2%)
3 Years	5	91	2.3% (0.0%, 5.4%)	6	142	1.7% (0.0%, 3.8%)	6	142	1.7% (0.0%, 3.8%)

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Table 77: Risk of First Occurrence of Irritation (>= Moderate Severity)

Time	By Patient				By Implant			
	Number Affected	Number Remaining	Cumulative Risk		Number Affected	Number Remaining	Cumulative Risk	
	n	n	% (95% CI)		n	n	% (95% CI)	
4 weeks	0	219	0.0%	--	0	358	0.0%	--
6 Months	0	205	0.0%	--	0	333	0.0%	--
1 Year	0	196	0.0%	--	0	317	0.0%	--
2 Years	0	182	0.0%	--	0	295	0.0%	--
3 Years	0	92	0.0%	--	0	143	0.0%	--

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Table 81: Risk of First Occurrence of Loss of Nipple Sensation

N/A: LOSS OF NIPPLE SENSATION HAS BEEN COMBINED WITH NIPPLE HYPERSENSITIVITY AND NIPPLE PARESTHESIA

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Table 85: Risk of First Occurrence of Loss of skin sensation

N/A: LOSS OF SKIN SENSATION HAS BEEN COMBINED WITH SKIN HYPERSENSITIVITY AND SKIN PARESTHESIA

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Table 89A: Risk of First Occurrence of Lymphadenopathy (>= Moderate Severity)

Time	By Patient				By Implant			
	Number Affected	Number Remaining	Cumulative Risk		Number Affected	Number Remaining	Cumulative Risk	
	n	n	% (95% CI)		n	n	% (95% CI)	
4 weeks	0	219	0.0%	--	0	358	0.0%	--
6 Months	0	205	0.0%	--	0	333	0.0%	--
1 Year	0	196	0.0%	--	0	317	0.0%	--
2 Years	0	182	0.0%	--	0	295	0.0%	--
3 Years	0	92	0.0%	--	0	143	0.0%	--

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Table 89B: Risk of First Occurrence of Lymphadenopathy (All severity Levels)

Time	By Patient				By Implant				
	Number Affected	Number Remaining	Cumulative Risk	Number Affected	Number Remaining	Cumulative Risk	Number Affected	Number Remaining	Cumulative Risk
	n	n	% (95% CI)	n	n	% (95% CI)	n	n	% (95% CI)
4 weeks	0	219	0.0%	0	358	0.0%	0	358	0.0%
6 Months	0	205	0.0%	0	333	0.0%	0	333	0.0%
1 Year	1	195	0.5% (0.0%, 1.5%)	1	316	0.3% (0.0%, 0.9%)	1	316	0.3% (0.0%, 0.9%)
2 Years	1	181	0.5% (0.0%, 1.5%)	1	294	0.3% (0.0%, 0.9%)	1	294	0.3% (0.0%, 0.9%)
3 Years	1	91	0.5% (0.0%, 1.9%)	1	142	0.3% (0.0%, 1.2%)	1	142	0.3% (0.0%, 1.2%)

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Table 93A: Risk of First Occurrence of Lymphedema (>= Moderate Severity)

Time	By Patient				By Implant			
	Number Affected	Number Remaining	Cumulative Risk	% (95% CI)	Number Affected	Number Remaining	Cumulative Risk	% (95% CI)
	n	n	%	(95% CI)	n	n	%	(95% CI)
4 weeks	0	219	0.0%	--	0	358	0.0%	--
6 Months	0	205	0.0%	--	0	333	0.0%	--
1 Year	0	196	0.0%	--	0	317	0.0%	--
2 Years	0	182	0.0%	--	0	295	0.0%	--
3 Years	0	92	0.0%	--	0	143	0.0%	--

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Table 93B: Risk of First Occurrence of Lymphedema (All severity Levels)

Time	By Patient				By Implant			
	Number Affected	Number Remaining	Cumulative Risk	% (95% CI)	Number Affected	Number Remaining	Cumulative Risk	% (95% CI)
	n	n			n	n		
4 weeks	0	219	0.0%	--	0	358	0.0%	--
6 Months	0	205	0.0%	--	0	333	0.0%	--
1 Year	0	196	0.0%	--	0	317	0.0%	--
2 Years	0	182	0.0%	--	0	295	0.0%	--
3 Years	1	91	1.0%	(0.0%, 3.0%)	1	142	0.6%	(0.0%, 1.9%)

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Table 97: Risk of First Occurrence of Nipple Hypersensitivity

N/A: NIPPLE HYPERSENSITIVITY HAS BEEN COMBINED WITH LOSS OF NIPPLE SENSATION AND NIPPLE PARESTHESIA

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Table 101: Risk of First Occurrence of Nipple Hypersensitivity / Paresthesia / Loss of Nipple Sensation (>= Moderate Severity)

Time	By Patient				By Implant			
	Number Affected	Number Remaining	Cumulative Risk	% (95% CI)	Number Affected	Number Remaining	Cumulative Risk	% (95% CI)
	n	n	%	(95% CI)	n	n	%	(95% CI)
4 Weeks	0	219	0.0%	--	0	358	0.0%	--
6 Months	0	205	0.0%	--	0	333	0.0%	--
1 Year	0	196	0.0%	--	0	317	0.0%	--
2 Years	0	182	0.0%	--	0	295	0.0%	--
3 Years	0	92	0.0%	--	0	143	0.0%	--

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Table 105A: Risk of First Occurrence of Hypertrophic / Other Abnormal Scarring (>= Moderate severity)

Time	By Patient				By Implant			
	Number Affected	Number Remaining	Cumulative Risk		Number Affected	Number Remaining	Cumulative Risk	
	n	n	% (95% CI)		n	n	% (95% CI)	
4 Weeks	0	219	0.0%		0	358	0.0%	--
6 Months	4	201	1.8% (0.0%, 3.7%)		5	329	1.4% (0.1%, 2.7%)	--
1 Year	6	190	2.8% (0.5%, 5.2%)		7	311	2.0% (0.5%, 3.6%)	
2 Years	7	175	3.4% (0.7%, 6.0%)		8	288	2.4% (0.6%, 4.1%)	
3 Years	7	89	3.4% (0.0%, 7.1%)		8	140	2.4% (0.0%, 4.8%)	

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Table 105B: Risk of First Occurrence of Hypertrophic / Other Abnormal Scarring (All Severity Levels)

Time	By Patient				By Implant			
	Number Affected	Number Remaining	Cumulative Risk		Number Affected	Number Remaining	Cumulative Risk	
	n	n	% (95% CI)		n	n	% (95% CI)	
4 weeks	1	218	0.5% (0.0%, 1.3%)		1	357	0.3% (0.0%, 0.8%)	
6 Months	6	200	2.8% (0.5%, 5.0%)		7	328	2.0% (0.5%, 3.5%)	
1 Year	7	190	3.3% (0.8%, 5.7%)		8	311	2.3% (0.6%, 3.9%)	
2 Years	10	173	4.8% (1.7%, 8.0%)		11	286	3.3% (1.2%, 5.3%)	
3 Years	12	88	6.0% (1.2%, 10.8%)		13	139	4.0% (0.8%, 7.2%)	

CORE STUDY - RECONSTRUCTION

Table 109A: Risk of First Occurrence of Other Nipple Related Observation (>= Moderate severity)

Time	By Patient				By Implant			
	Number Affected	Number Remaining	Cumulative Risk		Number Affected	Number Remaining	Cumulative Risk	
	n	n	% (95% CI)	n	n	% (95% CI)	n	% (95% CI)
4 weeks	1	218	0.5% (0.0%, 1.4%)	2	356	0.6% (0.0%, 1.3%)		
6 Months	3	202	1.4% (0.0%, 3.0%)	5	328	1.4% (0.1%, 2.7%)		
1 Year	7	189	3.4% (0.8%, 5.9%)	9	309	2.6% (0.9%, 4.4%)		
2 Years	9	175	4.4% (1.4%, 7.4%)	12	287	3.6% (1.5%, 5.7%)		
3 Years	9	87	4.4% (0.2%, 8.7%)	12	138	3.6% (0.5%, 6.7%)		

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Table 109B: Risk of First Occurrence of other Nipple Related Observation (All severity Levels)

Time	By Patient				By Implant			
	Number Affected		Cumulative Risk		Number Affected		Cumulative Risk	
	n	% (95% CI)						
4 weeks	4	1.8% (0.0%, 3.6%)	215	1.8% (0.0%, 3.6%)	5	1.4% (0.2%, 2.6%)	353	1.4% (0.2%, 2.6%)
6 Months	10	4.7% (1.8%, 7.5%)	195	4.7% (1.8%, 7.5%)	14	4.0% (1.9%, 6.1%)	319	4.0% (1.9%, 6.1%)
1 Year	15	7.1% (3.5%, 10.8%)	181	7.1% (3.5%, 10.8%)	19	5.5% (3.0%, 8.0%)	299	5.5% (3.0%, 8.0%)
2 Years	19	9.3% (5.0%, 13.5%)	165	9.3% (5.0%, 13.5%)	24	7.2% (4.2%, 10.1%)	275	7.2% (4.2%, 10.1%)
3 Years	19	9.3% (3.3%, 15.2%)	82	9.3% (3.3%, 15.2%)	24	7.2% (2.9%, 11.4%)	132	7.2% (2.9%, 11.4%)

CORE STUDY - RECONSTRUCTION

Table 113: Risk of First Occurrence of Pneumothorax (All Severity Levels)

Time	By Patient				By Implant			
	Number Affected	Number Remaining	Cumulative Risk		Number Affected	Number Remaining	Cumulative Risk	
	n	n	% (95% CI)		n	n	% (95% CI)	
4 weeks	0	219	0.0%	--	0	358	0.0%	--
6 Months	0	205	0.0%	--	0	333	0.0%	--
1 Year	1	195	0.5% (0.0%, 1.5%)		1	316	0.3% (0.0%, 0.9%)	
2 Years	1	181	0.5% (0.0%, 1.5%)		1	294	0.3% (0.0%, 0.9%)	
3 Years	1	92	0.5% (0.0%, 1.9%)		1	143	0.3% (0.0%, 1.2%)	

CORE STUDY - RECONSTRUCTION

Table II7A: Risk of First Occurrence of Ptosis (>= Moderate severity)

Time	By Patient				By Implant				
	Number Affected	Number Remaining	Cumulative Risk	Number Affected	Number Remaining	Cumulative Risk	Number Affected	Number Remaining	Cumulative Risk
	n	n	% (95% CI)	n	n	% (95% CI)	n	n	% (95% CI)
4 weeks	1	218	0.5% (0.0%, 1.3%)	1	357	0.3% (0.0%, 0.8%)	1	357	0.3% (0.0%, 0.8%)
6 Months	1	204	0.5% (0.0%, 1.4%)	1	333	0.3% (0.0%, 0.8%)	1	333	0.3% (0.0%, 0.8%)
1 Year	1	195	0.5% (0.0%, 1.4%)	1	317	0.3% (0.0%, 0.9%)	1	317	0.3% (0.0%, 0.9%)
2 Years	2	180	1.0% (0.0%, 2.4%)	2	294	0.6% (0.0%, 1.5%)	2	294	0.6% (0.0%, 1.5%)
3 Years	2	92	1.0% (0.0%, 3.0%)	2	143	0.6% (0.0%, 1.9%)	2	143	0.6% (0.0%, 1.9%)

CORE STUDY - RECONSTRUCTION

Table 117B: Risk of First Occurrence of Ptosis (All severity Levels)

Time	By Patient				By Implant			
	Number Affected	Number Remaining	Cumulative Risk	% (95% CI)	Number Affected	Number Remaining	Cumulative Risk	% (95% CI)
	n	n			n	n		
4 weeks	2	217	0.9%	(0.0%, 2.2%)	2	356	0.6%	(0.0%, 1.3%)
6 Months	2	203	0.9%	(0.0%, 2.2%)	2	332	0.6%	(0.0%, 1.4%)
1 Year	2	194	0.9%	(0.0%, 2.2%)	2	316	0.6%	(0.0%, 1.4%)
2 Years	3	179	1.4%	(0.0%, 3.2%)	3	293	0.9%	(0.0%, 1.9%)
3 Years	3	92	1.4%	(0.0%, 3.8%)	3	143	0.9%	(0.0%, 2.4%)

CORE STUDY - RECONSTRUCTION

Table 121A: Risk of First Occurrence of Redness (>= Moderate Severity)

Time	By Patient				By Implant				
	Number Affected	Number Remaining	Cumulative Risk	Number Affected	Number Remaining	Cumulative Risk	Number Affected	Number Remaining	Cumulative Risk
	n	n	% (95% CI)	n	n	% (95% CI)	n	n	% (95% CI)
4 Weeks	0	219	0.0%	0	358	0.0%	0	358	0.0%
6 Months	2	203	1.0% (0.0%, 2.3%)	2	331	0.6% (0.0%, 1.4%)	2	331	0.6% (0.0%, 1.5%)
1 Year	2	194	1.0% (0.0%, 2.3%)	2	315	0.6% (0.0%, 1.5%)	2	293	0.6% (0.0%, 1.5%)
2 Years	2	180	1.0% (0.0%, 2.4%)	2	293	0.6% (0.0%, 1.5%)	2	142	0.6% (0.0%, 1.5%)
3 Years	2	91	1.0% (0.0%, 3.0%)	2	142	0.6% (0.0%, 1.9%)	2	142	0.6% (0.0%, 1.9%)

CORE STUDY - RECONSTRUCTION

Table 121B: Risk of First Occurrence of Redness (All severity Levels)

Time	By Patient				By Implant			
	Number Affected	Number Remaining	Cumulative Risk		Number Affected	Number Remaining	Cumulative Risk	
	n	n	% (95% CI)		n	n	% (95% CI)	
4 weeks	1	218	0.5% (0.0%, 1.3%)		1	357	0.3% (0.0%, 0.8%)	
6 Months	8	197	3.7% (1.1%, 6.3%)		10	323	2.9% (1.1%, 4.7%)	
1 Year	9	188	4.3% (1.4%, 7.1%)		11	308	3.2% (1.2%, 5.1%)	
2 Years	13	170	6.4% (2.8%, 9.9%)		15	283	4.5% (2.1%, 6.8%)	
3 Years	13	84	6.4% (1.3%, 11.4%)		15	135	4.5% (1.1%, 7.9%)	

CORE STUDY - RECONSTRUCTION

Table 125A: Risk of First Occurrence of Seroma / Fluid Accumulation (>= Moderate Severity)

Time	By Patient				By Implant			
	Number Affected	Number Remaining	Cumulative Risk	% (95% CI)	Number Affected	Number Remaining	Cumulative Risk	% (95% CI)
	n	n	% (95% CI)		n	n	% (95% CI)	
4 Weeks	3	216	1.4% (0.0%, 2.9%)		3	355	0.8% (0.0%, 1.8%)	
6 Months	4	201	1.8% (0.0%, 3.7%)		4	329	1.1% (0.0%, 2.3%)	
1 Year	4	192	1.8% (0.0%, 3.7%)		4	313	1.1% (0.0%, 2.3%)	
2 Years	4	178	1.8% (0.0%, 3.8%)		4	291	1.1% (0.0%, 2.3%)	
3 Years	4	91	1.8% (0.0%, 4.5%)		4	142	1.1% (0.0%, 2.8%)	

CORE STUDY - RECONSTRUCTION

Table 125B: Risk of First Occurrence of Seroma / Fluid Accumulation (All Severity Levels)

Time	By Patient				By Implant			
	Number Affected	Number Remaining	Cumulative Risk	% (95% CI)	Number Affected	Number Remaining	Cumulative Risk	% (95% CI)
	n	n	%	(95% CI)	n	n	%	(95% CI)
4 weeks	9	210	4.1%	(1.5%, 6.7%)	10	348	2.8%	(1.1%, 4.5%)
6 Months	10	196	4.6%	(1.7%, 7.4%)	11	323	3.1%	(1.2%, 4.9%)
1 Year	10	188	4.6%	(1.6%, 7.5%)	11	308	3.1%	(1.2%, 5.0%)
2 Years	11	173	5.1%	(1.9%, 8.2%)	12	285	3.4%	(1.3%, 5.4%)
3 Years	11	89	5.1%	(0.6%, 9.5%)	12	140	3.4%	(0.4%, 6.3%)

CORE STUDY - RECONSTRUCTION

Table 129: Risk of First Occurrence of Skin Hypersensitivity

N/A: SKIN HYPERSENSITIVITY HAS BEEN COMBINED WITH LOSS OF SKIN SENSATION AND SKIN PARESTHESIA

CORE STUDY - RECONSTRUCTION

Table 133: Risk of First Occurrence of skin Hypersensitivity / Paresthesia / Loss of skin sensation (>= Moderate Severity)

Time	By Patient				By Implant			
	Number Affected	Number Remaining	Cumulative Risk	% (95% CI)	Number Affected	Number Remaining	Cumulative Risk	% (95% CI)
	n	n			n	n		
4 weeks	0	219	0.0%	--	0	358	0.0%	--
6 Months	0	205	0.0%	--	0	333	0.0%	--
1 Year	0	196	0.0%	--	0	317	0.0%	--
2 Years	0	182	0.0%	--	0	295	0.0%	--
3 Years	0	92	0.0%	--	0	143	0.0%	--

CORE STUDY - RECONSTRUCTION

Table 137A: Risk of First Occurrence of skin Rash (>= Moderate severity)

Time	By Patient				By Implant			
	Number Affected	Number Remaining	Cumulative Risk	% (95% CI)	Number Affected	Number Remaining	Cumulative Risk	% (95% CI)
	n	n			n	n		
4 weeks	3	216	1.4%	(0.0%, 2.9%)	4	354	1.1%	(0.0%, 2.2%)
6 Months	3	202	1.4%	(0.0%, 2.9%)	4	329	1.1%	(0.0%, 2.2%)
1 Year	3	193	1.4%	(0.0%, 3.0%)	4	313	1.1%	(0.0%, 2.3%)
2 Years	3	179	1.4%	(0.0%, 3.0%)	4	291	1.1%	(0.0%, 2.3%)
3 Years	3	91	1.4%	(0.0%, 3.7%)	4	142	1.1%	(0.0%, 2.8%)

CORE STUDY - RECONSTRUCTION

Table 137B: Risk of First Occurrence of Skin Rash (All Severity Levels)

Time	By Patient				By Implant			
	Number Affected	Number Remaining	Cumulative Risk	% (95% CI)	Number Affected	Number Remaining	Cumulative Risk	% (95% CI)
	n	n			n	n		
4 weeks	5	214	2.3%	(0.3%, 4.2%)	7	351	1.9%	(0.5%, 3.4%)
6 Months	6	199	2.7%	(0.5%, 5.0%)	9	324	2.5%	(0.8%, 4.2%)
1 Year	6	190	2.7%	(0.5%, 5.0%)	9	308	2.5%	(0.8%, 4.2%)
2 Years	6	177	2.7%	(0.4%, 5.1%)	9	288	2.5%	(0.7%, 4.3%)
3 Years	6	89	2.7%	(0.0%, 6.1%)	9	139	2.5%	(0.0%, 5.1%)

CORE STUDY - RECONSTRUCTION

Table 141A: Risk of First Occurrence of Swelling (>= Moderate Severity)

Time	By Patient				By Implant			
	Number Affected	Number Remaining	Cumulative Risk		Number Affected	Number Remaining	Cumulative Risk	
	n	n	% (95% CI)		n	n	% (95% CI)	
4 Weeks	7	212	3.2% (0.9%, 5.5%)		8	350	2.2% (0.7%, 3.7%)	
6 Months	8	200	3.7% (1.1%, 6.2%)		10	327	2.8% (1.0%, 4.6%)	
1 Year	8	191	3.7% (1.0%, 6.3%)		10	311	2.8% (1.0%, 4.6%)	
2 Years	8	177	3.7% (0.9%, 6.4%)		10	289	2.8% (0.9%, 4.7%)	
3 Years	8	90	3.7% (0.0%, 7.5%)		10	140	2.8% (0.1%, 5.5%)	

CORE STUDY - RECONSTRUCTION

Table 141B: Risk of First Occurrence of Swelling

Time	By Patient				By Implant			
	Number Affected	Number Remaining	Cumulative Risk	% (95% CI)	Number Affected	Number Remaining	Cumulative Risk	% (95% CI)
	n	n			n	n		
4 weeks	26	193	11.8%	(7.5%, 16.1%)	31	327	8.6%	(5.7%, 11.5%)
6 Months	35	177	16.0%	(11.0%, 20.9%)	40	302	11.2%	(7.8%, 14.5%)
1 Year	36	169	16.4%	(11.3%, 21.5%)	41	287	11.5%	(8.0%, 14.9%)
2 Years	36	157	16.4%	(11.1%, 21.7%)	41	267	11.5%	(7.9%, 15.1%)
3 Years	36	81	16.4%	(9.1%, 23.8%)	41	134	11.5%	(6.4%, 16.5%)

CORE STUDY - RECONSTRUCTION

Table 145A: Risk of First Occurrence of Tissue/Skin Necrosis (\geq Moderate Severity)

Time	By Patient				By Implant				
	Number Affected		Number Remaining		Number Affected		Number Remaining		Cumulative Risk (95% CI)
	n	%	n	%	n	%	n	%	
4 weeks	0	0.0%	219	0.0%	0	0.0%	358	0.0%	0.0%
6 Months	7	3.3%	198	3.3%	8	3.3%	326	2.3%	(0.7%, 3.9%)
1 Year	8	3.8%	188	3.8%	9	3.8%	310	2.6%	(0.9%, 4.3%)
2 Years	9	4.3%	173	4.3%	10	4.3%	288	2.9%	(1.0%, 4.8%)
3 Years	9	4.3%	84	4.3%	10	4.3%	138	2.9%	(0.2%, 5.7%)

CORE STUDY - RECONSTRUCTION

Table 145B: Risk of First Occurrence of Tissue/Skin Necrosis (All severity Levels)

Time	By Patient				By Implant			
	Number Affected	Number Remaining	Cumulative Risk	% (95% CI)	Number Affected	Number Remaining	Cumulative Risk	% (95% CI)
	n	n	% (95% CI)		n	n	% (95% CI)	
4 weeks	2	217	0.9% (0.0%, 2.2%)		2	356	0.6% (0.0%, 1.3%)	
6 Months	11	194	5.1% (2.1%, 8.1%)		12	322	3.4% (1.5%, 5.4%)	
1 Year	12	184	5.6% (2.4%, 8.8%)		14	305	4.0% (1.9%, 6.2%)	
2 Years	13	169	6.1% (2.6%, 9.6%)		15	283	4.4% (2.0%, 6.7%)	
3 Years	13	83	6.1% (1.1%, 11.1%)		15	136	4.4% (1.0%, 7.7%)	

CORE STUDY - RECONSTRUCTION

Table 149: Risk of First Occurrence of Wrinkling/Rippling (>= Moderate severity)

Time	By Patient				By Implant			
	Number Affected	Number Remaining	Cumulative Risk		Number Affected	Number Remaining	Cumulative Risk	
	n	n	% (95% CI)		n	n	% (95% CI)	
4 weeks	0	219	0.0%		0	358	0.0%	--
6 Months	4	201	1.9% (0.0%, 3.8%)		5	328	1.5% (0.2%, 2.7%)	
1 Year	6	191	2.9% (0.6%, 5.2%)		7	314	2.1% (0.5%, 3.6%)	
2 Years	6	177	2.9% (0.5%, 5.3%)		7	292	2.1% (0.5%, 3.7%)	
3 Years	7	89	3.5% (0.0%, 7.2%)		8	142	2.4% (0.0%, 4.9%)	

CORE STUDY - RECONSTRUCTION

Table 153A: Risk of First Occurrence of Other Complications (>= Moderate severity)

Time	By Patient				By Implant			
	Number Affected	Number Remaining	Cumulative Risk	% (95% CI)	Number Affected	Number Remaining	Cumulative Risk	% (95% CI)
	n	n	% (95% CI)		n	n	% (95% CI)	
4 weeks	0	219	0.0%	--	0	358	0.0%	--
6 months	1	204	0.5% (0.0%, 1.4%)		1	332	0.3% (0.0%, 0.9%)	
1 Year	1	195	0.5% (0.0%, 1.4%)		1	316	0.3% (0.0%, 0.9%)	
2 Years	1	181	0.5% (0.0%, 1.5%)		1	294	0.3% (0.0%, 0.9%)	
3 Years	1	92	0.5% (0.0%, 1.9%)		1	143	0.3% (0.0%, 1.2%)	

CORE STUDY - RECONSTRUCTION

Table 153A (Cont.): Risk of First Occurrence of Other Complications

Other Complications Specified (N = 1)

Pt Seq#	Other Complications Specified
001	MILD TO MODERATE VENOUS CONGESTION

CORE STUDY - RECONSTRUCTION

Table 153B: Risk of First Occurrence of Other Complications (All severity Levels)

Time	By Patient				By Implant			
	Number Affected	n	Number Remaining	Cumulative Risk % (95% CI)	Number Affected	n	Number Remaining	Cumulative Risk % (95% CI)
4 Weeks	0	219	0.0%	0.0%	0	358	0.0%	0.0%
6 Months	1	204	0.5%	0.5% (0.0%, 1.4%)	1	332	0.3%	0.3% (0.0%, 0.9%)
1 Year	1	195	0.5%	0.5% (0.0%, 1.4%)	1	316	0.3%	0.3% (0.0%, 0.9%)
2 Years	1	181	0.5%	0.5% (0.0%, 1.5%)	1	294	0.3%	0.3% (0.0%, 0.9%)
3 Years	1	92	0.5%	0.5% (0.0%, 1.9%)	1	143	0.3%	0.3% (0.0%, 1.2%)

CORE STUDY - RECONSTRUCTION

Table 153B (Cont.): Risk of First Occurrence of Other Complications (All Severity Levels)

Other Complications Specified (N = 1)

Pt

Seq# Other Complications Specified

001 MILD TO MODERATE VENOUS CONGESTION

CORE STUDY - RECONSTRUCTION

Table 160: Risk of First Occurrence of Implant Rupture

Time	By Patient				By Implant				
	Number Affected		Number Remaining		Number Affected		Number Remaining		Cumulative Risk (95% CI)
	n	%	n	%	n	%	n	%	
4 Weeks	0	0.0%	219	0.0%	0	0.0%	358	0.0%	--
6 Months	0	0.0%	205	0.0%	0	0.0%	333	0.0%	--
1 Year	0	0.0%	196	0.0%	0	0.0%	317	0.0%	--
2 Years	12	6.3%	170	6.3%	13	1.9%	282	4.2%	(1.9%, 6.5%)
3 Years	12	6.3%	85	6.3%	13	4.2%	138	4.2%	(0.9%, 7.5%)

CORE STUDY - RECONSTRUCTION

Table 163: Risk of First Occurrence of Reoperation

Time	By Patient				By Implant			
	Number Affected	Number Remaining	Cumulative Risk		Number Affected	Number Remaining	Cumulative Risk	
	n	n	% (95% CI)		n	n	% (95% CI)	
4 weeks	9	210	4.1% (1.5%, 6.7%)		9	349	2.5% (0.9%, 4.1%)	
6 Months	52	167	23.7% (18.1%, 29.4%)		69	289	19.3% (15.2%, 23.4%)	
1 Year	70	147	32.0% (25.8%, 38.2%)		93	261	26.0% (21.5%, 30.6%)	
2 Years	81	128	37.2% (30.6%, 43.8%)		107	235	30.1% (25.2%, 35.0%)	
3 Years	92	62	45.9% (36.8%, 55.1%)		124	113	38.2% (31.2%, 45.2%)	

CORE STUDY - RECONSTRUCTION

Table 171: Risk of First Occurrence of Implant Replacement/Removal

Time	By Patient				By Implant			
	Number Affected	Number Remaining	Cumulative Risk		Number Affected	Number Remaining	Cumulative Risk	
	n	n	% (95% CI)		n	n	% (95% CI)	
4 weeks	0	219	0.0%	--	0	358	0.0%	--
6 Months	19	199	8.7% (5.0%, 12.5%)		23	334	6.4% (3.9%, 9.0%)	
1 Year	29	187	13.3% (8.8%, 17.9%)		35	318	9.8% (6.7%, 12.9%)	
2 Years	36	170	16.6% (11.5%, 21.8%)		43	295	12.1% (8.6%, 15.6%)	
3 Years	46	78	25.3% (16.9%, 33.6%)		56	143	18.7% (12.9%, 24.5%)	

CORE STUDY - RECONSTRUCTION

Table 172: Risk of First Occurrence of Implant Removal with Replacement

Time	By Patient				By Implant			
	Number Affected	Number Remaining	Cumulative Risk		Number Affected	Number Remaining	Cumulative Risk	
	n	n	% (95% CI)		n	n	% (95% CI)	
4 Weeks	0	219	0.0%		0	358	0.0%	
6 Months	16	199	7.4% (3.9%, 10.9%)		20	334	5.6% (3.2%, 8.0%)	
1 Year	25	187	11.6% (7.3%, 15.9%)		31	318	8.8% (5.8%, 11.7%)	
2 Years	32	170	15.0% (10.1%, 19.9%)		39	295	11.1% (7.7%, 14.5%)	
3 Years	41	78	23.0% (14.8%, 31.2%)		51	143	17.2% (11.6%, 22.9%)	

CORE STUDY - RECONSTRUCTION

Table 173: Risk of First Occurrence of Implant Removal without Replacement

Time	By Patient				By Implant			
	Number Affected		Number Remaining		Number Affected		Number Remaining	
	n	% (95% CI)	n	% (95% CI)	n	% (95% CI)	n	% (95% CI)
4 weeks	0	0.0%	219	0.0%	0	0.0%	358	0.0%
6 Months	3	1.4% (0.0%, 3.0%)	201	1.4% (0.0%, 3.0%)	3	0.9% (0.0%, 1.8%)	333	0.9% (0.0%, 1.8%)
1 Year	4	1.9% (0.0%, 3.8%)	191	1.9% (0.0%, 3.8%)	4	1.2% (0.0%, 2.3%)	317	1.2% (0.0%, 2.3%)
2 Years	4	1.9% (0.0%, 3.9%)	175	1.9% (0.0%, 3.9%)	4	1.2% (0.0%, 2.4%)	295	1.2% (0.0%, 2.4%)
3 Years	5	3.0% (0.0%, 6.5%)	84	3.0% (0.0%, 6.5%)	5	1.8% (0.0%, 3.9%)	143	1.8% (0.0%, 3.9%)

CORE STUDY - RECONSTRUCTION

Table 178: Risk of First Occurrence of Any General Breast Surgery Complication

Time	By Patient				By Implant			
	Number Affected	Number Remaining	Cumulative Risk	% (95% CI)	Number Affected	Number Remaining	Cumulative Risk	% (95% CI)
	n	n	%	(95% CI)	n	n	%	(95% CI)
4 Weeks	57	162	25.9%	(20.1%, 31.7%)	70	288	19.4%	(15.3%, 23.5%)
6 Months	95	120	43.4%	(36.7%, 50.0%)	126	223	35.3%	(30.2%, 40.3%)
1 Year	103	106	47.3%	(40.3%, 54.2%)	136	201	38.2%	(33.0%, 43.5%)
2 Years	113	87	52.4%	(45.2%, 59.7%)	151	174	43.0%	(37.4%, 48.5%)
3 Years	118	48	56.2%	(46.9%, 65.5%)	159	92	46.9%	(39.4%, 54.3%)

CORE STUDY - RECONSTRUCTION

Table 179: Risk of First Occurrence of Any Breast Implant surgery: Cosmetic Complication

Time	By Patient				By Implant			
	Number Affected	Number Remaining	Cumulative Risk		Number Affected	Number Remaining	Cumulative Risk	
	n	n	% (95% CI)		n	n	% (95% CI)	
4 weeks	13	206	5.9% (2.8%, 9.0%)		14	344	3.9% (1.9%, 5.9%)	
6 Months	32	181	14.7% (9.9%, 19.5%)		40	308	11.3% (7.9%, 14.6%)	
1 Year	41	168	19.0% (13.6%, 24.3%)		49	293	13.9% (10.2%, 17.5%)	
2 Years	47	153	22.0% (16.2%, 27.7%)		54	272	15.4% (11.4%, 19.3%)	
3 Years	50	76	24.3% (15.9%, 32.7%)		58	133	17.1% (11.3%, 23.0%)	

CORE STUDY - RECONSTRUCTION

Table 180: Risk of First Occurrence of Any Breast Implant Surgery: NonCosmetic Complication

Time	By Patient				By Implant			
	Number Affected	Number Remaining	Cumulative Risk	% (95% CI)	Number Affected	Number Remaining	Cumulative Risk	% (95% CI)
	n	n			n	n		
4 weeks	4	215	1.8%	(0.0%, 3.6%)	5	353	1.4%	(0.2%, 2.6%)
6 Months	31	182	14.3%	(9.6%, 19.0%)	37	313	10.4%	(7.2%, 13.6%)
1 Year	48	162	22.4%	(16.7%, 28.0%)	61	283	17.4%	(13.4%, 21.4%)
2 Years	55	147	25.8%	(19.7%, 31.9%)	68	262	19.5%	(15.1%, 23.8%)
3 Years	65	68	34.1%	(25.0%, 43.3%)	82	124	26.2%	(19.6%, 32.9%)

CORE STUDY - RECONSTRUCTION

Table 168: Primary* Reason For Reoperation and Primary Procedure Performed

Reason	Patient Reoperations	
	n	%(N = 127)
Device Rupture	5	3.9%
Capsular Contracture	1	0.8%
Extrusion	9	7.1%
Necrosis	6	4.7%
Healing Related	1	0.8%
	1	0.8%
	1	0.8%
	2	1.6%
	1	0.8%
	6	4.7%
	4	3.1%
	1	0.8%
	6	4.7%
	1	0.8%

CORE STUDY - RECONSTRUCTION

Table 168 (cont.): Primary* Reason For Reoperation and Primary Procedure Performed

Reason	Patient Reoperations	
	n	%(N = 127)
Pain	2	1.6%
Unsatisfactory Cosmetic Result	22	17.3%
	9	7.1%
	2	1.6%
	25	19.7%
	3	2.4%
	6	4.7%
	1	0.8%
	2	1.6%
	1	0.8%
	1	0.8%
	2	1.6%
	2	1.6%
	1	0.8%
	1	0.8%
	2	1.6%
Total	127	100.0%

Sent: Tuesday, July 29, 2003 11:15 PM

DR. SAHAR DAWISHA EMAIL 7/18/03

I am having difficulty understanding the rupture information for the Core Study, as described in your response to Deficiency 3 (Attachments 7 and 8). I am unable to track each suspected implant rupture listed in Tables 158 and 159 with the information in Attachments 7 and 8. For example, I cannot track the 6 suspected augmentation MRI ruptures in Table 158 with the augmentation information in these Attachments, and it is unclear where these 6 suspected ruptures fall out in Table 159. Likewise, it is unclear what outcome there was to the 2 augmentation reoperations in Table 158, and where they appear in Table 159. If you could provide this information/explanation for each indication, especially by next week, it would be very helpful.

Additionally, here is an example of how I understand the Core Augmentation rupture information, with areas I am unclear about shown with a blank line. If you could fill in the blanks, and prepare a similar description for Core Reconstruction and Core Revision groups, that would be great:

Of the 987 Core Augmentation implants, 10 implants were initially suspected ruptured through 3 years of follow-up: 1 through explant/reoperation, 1 by physician exam (pain and tenderness following a motor vehicle accident), 2 through mammography, and 6 through MRI screening of a subset of 143 augmentation patients (275 devices) who underwent MRI screening for rupture at approximately 1 year following implantation. These 6 suspected implant ruptures through MRI screening were not clinically evident--considered "silent ruptures"--and at initial MRI screening. Of the 6 suspected ruptures via MRI, ____ were determined to have "evidence of MRI rupture" and ____ were "indeterminate for MRI rupture." Follow-up evaluation of these 6 possible silent ruptures is as follows: for the ____ implants indicating evidence of rupture on initial MRI screening, ____ were confirmed intact by both follow-up mammogram and subsequent MRI screening indicating lack of rupture, and ____ was determined intact by follow-up ultrasound; for the ____ implants rated indeterminate for rupture at initial MRI screening, additional follow-up has not yet been performed. Therefore, there is confirmed rupture via explantation of 2 implants, and the ____ with "indeterminate rupture" status from MRI remain indeterminate. Therefore, there are 5 implant ruptures (3 confirmed and 2 unconfirmed) in 5 Core Augmentation patients through 3 years of follow-up.

Response to Deficiency 3 Question

The following information is provided to address the above questions for each cohort of the Core Clinical Study. In addition, a new Attachment 7 presents revised tables for confirmed ruptures, suspected ruptures, and confirmed non-ruptures in each cohort. These tables now include a new second column that identifies the diagnostic tool, e.g. MRI, physical exam, etc., by which ruptures may have been initially suspected. The detailed patient chronologies may now be tracked from the categories in Table 158 through Table 160 for each of the respective three cohorts.

Augmentation Cohort Core Clinical Study, Reports of Rupture

Of the 987 Core Augmentation implants, 10 implants were initially suspected ruptured through 3 years of follow-up (Reference PMA P020056, Amendment 3 [dated June 12, 2003], Volume 2, Table 158, page 200):

- 3 via Explant/reoperation
- 1 via Physician exam (breast pain following a motor vehicle accident); and
- 6 via MRI screening of a subset of augmentation patients who underwent MRI screening for rupture at approximately 1 year following implantation

The 6 suspected implant ruptures identified through MRI screening were not clinically evident, i.e. they could be considered “silent ruptures.” Of these 6 suspected silent ruptures, 2 were determined to have “evidence of rupture” and 4 were categorized as “indeterminate for rupture.” For those identified as indeterminate, patients underwent additional evaluation via ultrasound, mammogram or a second MRI. Results of these additional evaluations indicated no evidence of rupture in 2 implants. The other 2 implants continued to be classified as indeterminate at the time of the 3/27/03 data extract; however, additional information received since that time demonstrates that follow-up MRIs identified no evidence of rupture. For consistency with PMA Amendment 3, these 2 implants currently still appear in Table 159 as “unconfirmed” ruptures.

Follow-up evaluation of the 6 possible silent ruptures was reported as follows:

- For the 2 implants indicating evidence of rupture on initial MRI screening,
 - 1 was determined intact by both follow-up ultrasound and subsequent MRI screening indicating lack of rupture; and
 - 1 remains “unconfirmed” in the data tables, but has since been confirmed after the 3-year data extract to be ruptured via explant.
- For the 4 implants rated indeterminate for rupture at initial MRI screening,
 - 2 were determined intact by both follow-up mammogram and subsequent MRI screening indicating lack of rupture; and
 - 2 remain “unconfirmed” in the data tables, but have since been determined by follow-up MRI to be intact and non-ruptured

Through 3 years of follow-up, there are 2 confirmed ruptures via explantation, and 3 suspected ruptures remain unconfirmed in the data tables. (As noted above, since the 3-year data extract, 1 of the suspected ruptures has been confirmed to be ruptured via explant, and 2 other suspected ruptures have been confirmed via MRI to be non-ruptures. All 3 of these ruptures currently remain in the data tables as “unconfirmed”.) Therefore, at the time of 3-year data extract there are 5 implant ruptures (2 confirmed and 3 unconfirmed) in 5 Core Augmentation patients through 3 years of follow-up.

Reconstruction Cohort Core Clinical Study, Reports of Rupture

Of the 361 Core Reconstruction implants, 15 implants were initially suspected ruptured through 3 years of follow-up (Reference PMA P020056, Amendment 3 [dated June 12, 2003], Volume 3, Table 158, page 201):

- 1 via Explant
- 2 via Ultrasound
- 3 via Unknown diagnostic tools; and
- 9 via MRI screening of a subset of reconstruction patients who underwent MRI screening for rupture at approximately 1 year following implantation

The 9 suspected implant ruptures identified through MRI screening were not clinically evident, i.e. they could be considered “silent ruptures.” Of these 9 suspected silent ruptures, all 9 were determined to have “evidence of rupture.”

Follow-up evaluation of the 9 possible silent ruptures was reported as follows:

- 6 were confirmed ruptured at explant,
- 1 was confirmed not ruptured at explant,
- 1 is pending a second MRI; and
- 1 indicated evidence of rupture in a second MRI, but the patient is asymptomatic and the physician believes the implant is folded, not ruptured. Therefore, no additional follow-up is currently planned.

Through 3 years of follow-up, there are 8 confirmed ruptures via explantation, and 5 suspected implant ruptures remain unconfirmed at the time of 3-year data extract. Therefore, there are 13 implant ruptures (8 confirmed and 5 unconfirmed) in 12 Core Reconstruction patients through 3 years of follow-up.

Revision Cohort Core Clinical Study, Reports of Rupture

Of the 432 Core Revision implants, 12 implants were initially suspected ruptured through 3 years of follow-up (Reference PMA P020056, Amendment 3 [dated June 12, 2003], Volume 4, Table 158, page 201):

- 3 via Explant/reoperation
- 4 via Physician exam (significant change in implant feel, implant malposition, etc.)
- 1 via Ultrasound; and
- 4 via MRI screening of a subset of revision patients who underwent MRI screening for rupture at approximately 1 year following implantation

The 4 suspected implant ruptures identified through MRI screening were not clinically evident, i.e. they could be considered “silent ruptures.” Of these 4 suspected silent ruptures, all 4 were determined to have “evidence of rupture.”

Follow-up evaluation of the 4 possible silent ruptures was reported as follows:

- 3 were confirmed ruptured at explant; and
- 1 indicated evidence of rupture in a second MRI, but the patient is asymptomatic and the physician believes the implant is folded, not ruptured. Therefore, no additional follow-up is currently planned.

Through 3 years of follow-up, there are 5 confirmed ruptures via explantation, and 3 suspected implant ruptures remain unconfirmed. Therefore, there are 8 implant ruptures (5 confirmed and 3 unconfirmed) in 7 Core Revision patients through 3 years of follow-up.

Core Clinical Study Rupture Tables

Rupture Tables Are Organized in the Following Sequence:

- ❖ *Confirmed Ruptures - PMA**
- ❖ *Confirmed Ruptures - Updated Data***
- ❖ *Suspected Ruptures (Unconfirmed Ruptures) - PMA**
- ❖ *Suspected Ruptures (Unconfirmed Ruptures) - Updated Data***
- ❖ *Confirmed Non-Ruptures (False Reports) - PMA**
- ❖ *Confirmed Non-Ruptures (False Reports) - Updated Data***

*Reported in Module 5 of PMA, 12/27/02

**Reported in Amendment 3 to PMA, 6/12/03

Core Clinical Study

Rupture Tables

Augmentation Cohort

CORE STUDY - AUGMENTATION

Confirmed Implant Ruptures Reported in PMA

Patient ID	Rupture Suspected Via	Timing of Suspected Rupture Onset	Date of Rupture Confirmation	Implant Status	Details (symptoms and screening method with results)
Right Implant	Reoperation	8/1/99 (estimated)	10/20/99	Confirmed ruptured at explant	<ul style="list-style-type: none"> ▪ Implanted 5/13/99 ▪ Capsular contracture, Baker grade IV, noted on 10/4/99 ▪ Full capsulectomy on 10/20/99 revealed gel on implant surface ▪ Explant done same day (10/20/99)
Left Implant	Explant	12/6/99 (estimated)	7/13/00	Confirmed ruptured at explant	<ul style="list-style-type: none"> ▪ Implanted 5/1/99 ▪ Lump found by breast exam on 10/18/99 suspected to be rupture ▪ Mammogram and sonogram on 11/16/99 ruled out rupture (was swollen lymph node) ▪ Explant 7/13/00 for asymmetry and capsular contracture revealed evidence of rupture

CORE STUDY - AUGMENTATION

Confirmed Implant Ruptures - Updated Data

There were no confirmed implant ruptures identified after PMA submission among Augmentation patients.

CORE STUDY - AUGMENTATION

Suspected Implant Ruptures (Unconfirmed Ruptures) Reported in PMA

Patient ID	Rupture Suspected Via	Timing of Suspected Rupture Onset	Implant Status	Details (symptoms and screening method with results)	Proposed Action Plan to Confirm Rupture
Left Implant	MRI	1/9/01 (estimated)	Unconfirmed*	<ul style="list-style-type: none"> ▪ Implanted 1/4/00 ▪ MRI obtained 1/15/02 ▪ MRI indeterminate ▪ Second MRI obtained 2/10/03 ▪ MRI indicated no evidence of rupture* 	No further follow-up planned.
Left Implant	MRI	12/3/00 (estimated)	Unconfirmed*	<ul style="list-style-type: none"> ▪ Implanted 11/22/99 ▪ MRI obtained 12/15/01 ▪ MRI indeterminate ▪ Second MRI obtained 2/22/03 ▪ MRI indicated no evidence of rupture* 	No further follow-up planned.

*Case report form documenting second MRI was received after the 3/27/03 data extract, so patient appears on Table 159 as unconfirmed rupture status

CORE STUDY - AUGMENTATION

Suspected Implant Ruptures (Unconfirmed Ruptures) - Updated Data

Patient ID	Rupture Suspected Via	Timing of Suspected Rupture Onset	Implant Status	Details (symptoms and screening method with results)	Proposed Action Plan to Confirm Rupture
Left Implant	MRI	2/14/02 (estimated)	Unconfirmed*	<ul style="list-style-type: none"> ▪ Implanted 7/1/99 ▪ MRI obtained 8/31/02 ▪ MRI indicated evidence of rupture ▪ Explanted 9/6/02* ▪ Explant revealed evidence of rupture 	Explanted.

*Case report form documenting explant was received after the 3/27/03 data extract, so patient appears on Table 159 as unconfirmed rupture status

CORE STUDY - AUGMENTATION

Confirmed Implant Non-Ruptures (False Reports) Reported in PMA

Patient ID	Rupture Suspected Via	Date of Non-Rupture Confirmation	Implant Status	Details (symptoms and screening method with results)
Left Implant	Reoperation	10/20/99	Confirmed non-ruptured at explant	<ul style="list-style-type: none"> ▪ Implanted 5/13/99 ▪ Capsular contracture, Baker grade IV, noted on 10/4/99 ▪ Full capsulectomy on 10/20/99 ▪ Explant done same day (10/20/99)
Left Implant	Physician Exam	9/23/99	Confirmed non-ruptured by mammogram	<ul style="list-style-type: none"> ▪ Implanted 3/19/99 ▪ Patient experienced breast pain after motor vehicle accident ▪ Mammogram obtained 9/23/99 determined implant intact
Right Implant	MRI	10/21/01	Confirmed non-ruptured by ultrasound Reconfirmed non-ruptured by second MRI	<ul style="list-style-type: none"> ▪ Implanted 2/16/99 ▪ MRI obtained on 5/21/01 ▪ MRI indicated evidence of rupture according to MRI facility radiologist, but no rupture according to Central Reviewer ▪ Ultrasound obtained on 10/21/01 determined implant intact ▪ Second MRI obtained 4/8/02 ▪ MRI indicated no evidence of rupture

CORE STUDY - AUGMENTATION

Confirmed Implant Non-Ruptures (False Reports) Reported in PMA (cont.)

Patient ID	Rupture Suspected Via	Date of Non-Rupture Confirmation	Implant Status	Details (symptoms and screening method with results)
Left Implant	MRI	11/28/01	Confirmed non-ruptured by mammogram Reconfirmed non-ruptured by second MRI	<ul style="list-style-type: none"> ▪ Implanted 4/30/99 ▪ MRI obtained on 5/22/01 ▪ MRI indeterminate ▪ Mammogram obtained on 11/28/01 determined implant intact ▪ Second MRI obtained 6/17/02 ▪ MRI indicated no evidence of rupture
Right Implant	MRI	11/28/01	Confirmed non-ruptured by mammogram Reconfirmed non-ruptured by second MRI	<ul style="list-style-type: none"> ▪ Implanted 4/30/99 ▪ MRI obtained on 5/22/01 ▪ MRI indeterminate ▪ Mammogram obtained on 11/28/01 determined implant intact ▪ Second MRI obtained 6/17/02 ▪ MRI indicated no evidence of rupture

CORE STUDY - AUGMENTATION

Confirmed Implant Non-Ruptures (False Reports) - Updated Data

There were no confirmed implant non-ruptures identified after PMA submission among Augmentation patients.

Core Clinical Study

Rupture Tables

Reconstruction Cohort

CORE STUDY - RECONSTRUCTION

Confirmed Implant Ruptures Reported in PMA

Patient ID	Rupture Suspected Via	Timing of Suspected Rupture Onset	Date of Rupture Confirmation	Implant Status	Details (symptoms and screening method with results)
Left Implant	MRI	3/17/01 (estimated)	9/17/02	Confirmed ruptured at explant	<ul style="list-style-type: none"> ▪ Implanted 10/18/99 ▪ MRI obtained on 8/16/02 ▪ MRI indicated evidence of rupture ▪ Explanted 9/17/02 ▪ Note: previously reported in PMA as unconfirmed rupture
Right Implant	MRI	4/12/01 (estimated)	11/1/02	Confirmed ruptured at explant	<ul style="list-style-type: none"> ▪ Implanted 12/16/99 ▪ MRI obtained 8/9/02 ▪ MRI indicated evidence of rupture ▪ Explanted 11/1/02 ▪ Note: previously reported in PMA as unconfirmed rupture
Right Implant	MRI	4/17/01 (estimated)	9/17/02	Confirmed ruptured at explant	<ul style="list-style-type: none"> ▪ Implanted 12/14/99 ▪ MRI obtained 8/20/02 ▪ MRI indicated evidence of rupture ▪ Explanted 9/17/02 ▪ Note: previously reported in PMA as unconfirmed rupture
Right Implant	MRI	10/27/00 (estimated)	9/16/02	Confirmed ruptured at explant	<ul style="list-style-type: none"> ▪ Implanted 5/19/99 ▪ MRI obtained 4/8/02 ▪ MRI indicated evidence of rupture ▪ Explanted 9/16/02 ▪ Note: previously reported in PMA as unconfirmed rupture

CORE STUDY - RECONSTRUCTION

Confirmed Implant Ruptures Reported in PMA (cont.)

Patient ID	Rupture Suspected Via	Timing of Suspected Rupture Onset	Date of Rupture Confirmation	Implant Status	Details (symptoms and screening method with results)
Left Implant	MRI	3/16/01 (estimated)	7/26/02	Confirmed ruptured at explant	<ul style="list-style-type: none"> ▪ Implanted 2/9/00 ▪ MRI obtained 4/22/02 ▪ MRI indicated evidence of rupture ▪ Explanted 7/26/02
Right Implant	MRI	6/20/01 (estimated)	11/13/02	Confirmed ruptured at explant	<ul style="list-style-type: none"> ▪ Implanted 6/12/00 ▪ MRI obtained 6/28/02 ▪ MRI indicated evidence of rupture ▪ Explanted 11/13/02 ▪ Note: previously reported in PMA as unconfirmed rupture
Right Implant	Ultrasound	5/6/01 (estimated)	8/9/02	Confirmed ruptured at explant	<ul style="list-style-type: none"> ▪ Implanted 4/7/00 ▪ Patient complained of asymmetry on 6/4/02 ▪ Ultrasound obtained 6/4/02 ▪ Ultrasound indeterminate for rupture ▪ Explanted 8/9/02

CORE STUDY - RECONSTRUCTION

Confirmed Implant Ruptures - Updated Data

Patient ID	Rupture Suspected Via	Timing of Suspected Rupture Onset	Date of Rupture Confirmation	Implant Status	Details (symptoms and screening method with results)
Right Implant	Explant	5/13/01 (estimated)	12/6/02	Confirmed ruptured at explant	<ul style="list-style-type: none"> ▪ Implanted 12/9/99 ▪ MRI done 11/14/02* ▪ MRI indicated evidence of rupture ▪ Explanted 12/6/02

*MRI report obtained after the 3/27/03 data extract, so timing of suspected rupture onset has not yet been adjusted to reflect an earlier indication of rupture, based on the MRI date

CORE STUDY - RECONSTRUCTION

Suspected Implant Ruptures (Unconfirmed Ruptures) Reported in PMA

Patient ID	Rupture Suspected Via	Timing of Suspected Rupture Onset	Implant Status	Details (symptoms and screening method with results)	Proposed Action Plan to Confirm Rupture
Left Implant	MRI	10/7/00 (estimated)	Unconfirmed	<ul style="list-style-type: none"> ▪ Implanted 3/1/99 ▪ MRI obtained 5/17/02 ▪ MRI indicated evidence of rupture ▪ Second MRI obtained 3/4/03 ▪ MRI indicated evidence of rupture ▪ Patient asymptomatic 	No follow-up planned. Doctor believes implant is folded, not ruptured.
Left Implant	MRI	12/25/00 (estimated)	Unconfirmed	<ul style="list-style-type: none"> ▪ Implanted 5/24/99 ▪ MRI obtained 7/29/02 ▪ MRI indicated evidence of rupture ▪ Patient asymptomatic 	Additional MRI planned for July of 2003, one year after first MRI.

CORE STUDY - RECONSTRUCTION

Suspected Implant Ruptures (Unconfirmed Ruptures) - Updated Data

Patient ID	Rupture Suspected Via	Timing of Suspected Rupture Onset	Implant Status	Details (symptoms and screening method with results)	Proposed Action Plan to Confirm Rupture
Left Implant	Unknown (subsequently found to be Physician Exam)	6/28/01 (estimated)	Unconfirmed*	<ul style="list-style-type: none"> ▪ Implanted 12/17/99 ▪ Rupture suspected at follow up visit 1/8/03 due to change in breast shape ▪ MRI obtained on 1/29/03 ▪ MRI indicated no evidence of rupture ▪ Explanted 3/24/03* ▪ Explant revealed no evidence of rupture 	Explanted.
Left implant	Unknown (subsequently found to be MRI)	6/18/01 (estimated)	Unconfirmed*	<ul style="list-style-type: none"> ▪ Implanted 4/10/00 ▪ MRI obtained on 8/27/02 ▪ MRI indicated evidence of rupture according to MRI facility radiologist, but no rupture according to Central Reviewer ▪ Second evaluation of MRI films (after notification that implant was a double lumen) indicated no evidence of rupture* 	No further follow-up planned.
Right implant	Unknown (subsequently found to be MRI)	6/18/01 (estimated)	Unconfirmed*	<ul style="list-style-type: none"> ▪ Implanted 4/10/00 ▪ MRI obtained on 8/27/02 ▪ MRI indicated evidence of rupture according to MRI facility radiologist, but no rupture according to Central Reviewer ▪ Second evaluation of MRI films (after notification that implant was a double lumen) indicated no evidence of rupture* 	No further follow-up planned.

*Case report form documenting non-rupture was received after the 3/27/03 data extract, so patient appears on Table 159 as unconfirmed rupture status

CORE STUDY - RECONSTRUCTION

Confirmed Implant Non-Ruptures (False Reports) Reported in PMA

Patient ID	Rupture Suspected Via	Date of Non-Rupture Confirmation	Implant Status	Details (symptoms and screening method with results)
Left Implant	MRI	9/16/02	Confirmed non-ruptured at explant	<ul style="list-style-type: none"> ▪ Implanted 5/19/99 ▪ MRI obtained on 4/8/02 ▪ MRI indicated evidence of rupture ▪ Explanted 9/16/02 ▪ Note: previously reported in PMA as unconfirmed rupture
Right Implant	Ultrasound	8/9/02	Confirmed non-ruptured at explant	<ul style="list-style-type: none"> ▪ Implanted 4/7/00 ▪ Patient complained of asymmetry on 6/4/02 ▪ Ultrasound obtained 6/4/02 ▪ Ultrasound indeterminate for rupture ▪ Explanted 8/9/02

CORE STUDY - RECONSTRUCTION

Confirmed Implant Non-Ruptures (False Reports) - Updated Data

There were no confirmed implant non-ruptures identified after PMA submission among Reconstruction patients.

Core Clinical Study

Rupture Tables

Revision Cohort

CORE STUDY - REVISION

Confirmed Implant Ruptures Reported in PMA

Patient ID	Rupture Suspected Via	Timing of Suspected Rupture Onset	Date of Rupture Confirmation	Implant Status	Details (symptoms and screening method with results)
Left Implant	Physician Exam	4/18/01	4/23/01	Confirmed ruptured at explant	<ul style="list-style-type: none"> ▪ Implanted 11/18/99 ▪ Patient reported significant change in implant feel on 4/18/01, PI suspected rupture ▪ Explanted 4/23/01
Left Implant	MRI	11/14/00 (estimated)	7/17/02	Confirmed ruptured at explant	<ul style="list-style-type: none"> ▪ Implanted 4/20/99 ▪ MRI obtained 6/12/02 ▪ MRI indicated rupture ▪ Explanted 7/17/02
Left Implant	MRI	6/22/01 (estimated)	9/24/02	Confirmed ruptured at explant	<ul style="list-style-type: none"> ▪ Implanted 5/16/00 ▪ MRI obtained 7/29/02 ▪ MRI indicated evidence of rupture ▪ Explanted 9/24/02 ▪ Note: previously reported in PMA as unconfirmed rupture
Right Implant	MRI	12/6/00 (estimated)	10/11/02	Confirmed ruptured at explant	<ul style="list-style-type: none"> ▪ Implanted 4/7/99 ▪ MRI obtained 8/8/02 ▪ MRI indicated evidence of rupture ▪ Explanted 10/11/02 ▪ Note: previously reported in PMA as unconfirmed rupture

CORE STUDY - REVISION

Confirmed Implant Ruptures - Updated Data

Patient ID	Rupture Suspected Via	Timing of Suspected Rupture Onset	Date of Rupture Confirmation	Implant Status	Details (symptoms and screening method with results)
Right Implant	Reoperation	12/23/00 (estimated)	1/13/03	Confirmed ruptured at explant	<ul style="list-style-type: none">▪ Implanted 3/31/99▪ MRI obtained 6/18/02*▪ MRI indicated rupture▪ Explanted 1/13/03

*MRI report obtained after the 3/27/03 data extract, so timing of suspected rupture onset has not yet been adjusted to reflect an earlier indication of rupture, based on the MRI date

CORE STUDY - REVISION

Suspected Implant Ruptures (Unconfirmed Ruptures) Reported in PMA

Patient ID	Rupture Suspected Via	Timing of Suspected Rupture Onset	Implant Status	Details (symptoms and screening method with results)	Proposed Action Plan to Confirm Rupture
Left Implant	MRI	2/21/01 (estimated)	Unconfirmed	<ul style="list-style-type: none"> ▪ Implanted 1/31/00 ▪ MRI obtained 3/15/02 ▪ MRI indicated evidence of rupture ▪ Patient asymptomatic 	No follow-up planned. Doctor believes implant is folded, not ruptured.
Left Implant	Explant	9/28/00 (estimated)	Unconfirmed	<ul style="list-style-type: none"> ▪ Implanted 6/10/99 ▪ Patient had nodules in left breast ▪ Ultrasound obtained 9/20/01* ▪ Ultrasound indicates evidence of rupture ▪ Explanted 1/18/02 by another (unknown) surgeon due to suspected rupture ▪ Rupture status of implant unknown 	N/A
Right Implant	Explant	9/28/00 (estimated)	Unconfirmed	<ul style="list-style-type: none"> ▪ Implanted 6/10/99 ▪ Patient asymptomatic on right side ▪ Ultrasound obtained 9/20/01* ▪ Ultrasound indicates no evidence of rupture ▪ Explanted 1/18/02 by another (unknown) surgeon due to suspected rupture ▪ Rupture status of implant unknown 	N/A

*ultrasound report obtained after the 3/27/03 data extract, so timing of suspected rupture onset has not yet been adjusted to reflect an earlier indication of rupture, based on the ultrasound date

CORE STUDY - REVISION

Suspected Implant Ruptures (Unconfirmed Ruptures) - Updated Data

There were no suspected implant ruptures identified after PMA submission among Revision patients.

CORE STUDY - REVISION

Confirmed Implant Non-Ruptures (False Reports) Reported in PMA

Patient ID	Rupture Suspected Via	Date of Non-Rupture Confirmation	Implant Status	Details (symptoms and screening method with results)
Right Implant	Physician Exam	3/11/02	Confirmed non-ruptured by MRI	<ul style="list-style-type: none"> ▪ Implanted 6/10/99 ▪ Patient reported breast pain, implant malposition, palpability and wrinkling on 12/4/01 ▪ Ultrasound obtained on 2/25/02 ▪ Ultrasound indicated rupture ▪ MRI obtained 3/11/02 ▪ MRI indicated no evidence of rupture ▪ Symptoms determined to be related to pregnancy ▪ Patient reported absence of symptoms after pregnancy ended
Left Implant	Physician Exam	7/10/00	Confirmed non-ruptured at explant	<ul style="list-style-type: none"> ▪ Implanted 4/19/99 ▪ Physician exam on 4/20/00 showed left breast softer than right ▪ MRI obtained 7/3/00 ▪ MRI indeterminate for rupture ▪ Explanted 7/10/00
Right Implant	Physician Exam	5/11/99	Confirmed non-ruptured by MRI	<ul style="list-style-type: none"> ▪ Implanted 3/25/99 ▪ Physician exam on 5/11/99 showed right breast rippling and change in size ▪ MRI obtained 5/11/99 ▪ MRI indicated no rupture

CORE STUDY - REVISION

Confirmed Implant Non-Ruptures (False Reports) Reported in PMA (cont.)

Patient ID	Rupture Suspected Via	Date of Non-Rupture Confirmation	Implant Status	Details (symptoms and screening method with results)
Right Implant	Ultrasound	5/29/01	Confirmed non-ruptured at explant	<ul style="list-style-type: none">▪ Implanted 3/9/99▪ Patient reported itching in right breast on 5/25/01▪ Ultrasound obtained 5/25/01▪ Ultrasound indicated rupture▪ Explanted 5/29/01

CORE STUDY - REVISION

Confirmed Implant Non-Ruptures (False Reports) - Updated Data

There were no confirmed implant non-ruptures identified after PMA submission among Revision patients.

Sent: Friday, August 01, 2003 5:32 PM

CORE STUDY - REVISION

Confirmed Implant Non-Ruptures (False Reports) Reported in PMA

Patient ID	Rupture Suspected Via	Date of Non-Rupture Confirmation	Implant Status	Details (symptoms and screening method with results)
Right Implant	Physician Exam	3/11/02	Confirmed non-ruptured by MRI	<ul style="list-style-type: none">Implanted 6/10/99Patient reported breast pain, implant malposition, palpability and wrinkling on 12/4/01Ultrasound obtained on 2/25/02Ultrasound indicated ruptureMRI obtained 3/11/02MRI indicated no evidence of rupture
Left Implant	Physician Exam	7/10/00	Confirmed non-ruptured at explant	<ul style="list-style-type: none">Implanted 4/19/99Physician exam on 4/20/00 showed left breast softer than rightMRI obtained 6/14/00MRI indeterminate for ruptureExplanted 7/10/00
Right Implant	Physician Exam	5/21/99	Confirmed non-ruptured by MRI	<ul style="list-style-type: none">Implanted 3/25/99Physician exam on 5/11/99 showed right breast rippling and change in sizeMRI obtained 5/21/99MRI indicated no rupture

CORE STUDY - REVISION

Confirmed Implant Non-Ruptures (False Reports) Reported in PMA (cont.)

Patient ID	Rupture Suspected Via	Date of Non-Rupture Confirmation	Implant Status	Details (symptoms and screening method with results)
Right Implant	Ultrasound	5/29/01	Confirmed non-ruptured at explant	<ul style="list-style-type: none"> ▪ Implanted 3/9/99 ▪ Patient reported itching in right breast on 5/25/01 ▪ Ultrasound obtained 5/25/01 ▪ Ultrasound indicated rupture ▪ Explanted 5/29/01

CORE STUDY - REVISION

Confirmed Implant Non-Ruptures (False Reports) - Updated Data

There were no confirmed implant non-ruptures identified after PMA submission among Revision patients.

CORE STUDY - AUGMENTATION

Confirmed Implant Non-Ruptures (False Reports) Reported in PMA

Patient ID	Rupture Suspected Via	Date of Non-Rupture Confirmation	Implant Status	Details (symptoms and screening method with results)
Left Implant	Reoperation	10/20/99	Confirmed non-ruptured at explant	<ul style="list-style-type: none"> ▪ Implanted 5/13/99 ▪ Capsular contracture, Baker grade IV, noted on 10/4/99 ▪ Full capsulectomy on 10/20/99 ▪ Explant done same day (10/20/99)
Left Implant	Physician Exam	9/23/99	Confirmed non-ruptured by mammogram	<ul style="list-style-type: none"> ▪ Implanted 3/19/99 ▪ Patient experienced breast pain after motor vehicle accident ▪ Mammogram obtained 9/23/99 determined implant intact
Right Implant	MRI	10/12/01	Confirmed non-ruptured by ultrasound Reconfirmed non-ruptured by second MRI	<ul style="list-style-type: none"> ▪ Implanted 2/16/99 ▪ MRI obtained on 5/21/01 ▪ MRI indicated evidence of rupture according to MRI facility radiologist, but no rupture according to Central Reviewer ▪ Ultrasound obtained on 10/12/01 determined implant intact ▪ Second MRI obtained 4/8/02 ▪ MRI indicated no evidence of rupture

CORE STUDY - AUGMENTATION

Confirmed Implant Non-Ruptures (False Reports) Reported in PMA (cont.)

Patient ID	Rupture Suspected Via	Date of Non-Rupture Confirmation	Implant status	Details (symptoms and screening method with results)
Left Implant	MRI	11/28/01	Confirmed non-ruptured by mammogram Reconfirmed non-ruptured by second MRI	<ul style="list-style-type: none"> ▪ Implanted 4/30/99 ▪ MRI obtained on 5/22/01 ▪ MRI indeterminate ▪ Mammogram obtained on 11/28/01 determined implant intact ▪ Second MRI obtained 6/17/02 ▪ MRI indicated no evidence of rupture
Right Implant	MRI	11/28/01	Confirmed non-ruptured by mammogram Reconfirmed non-ruptured by second MRI	<ul style="list-style-type: none"> ▪ Implanted 4/30/99 ▪ MRI obtained on 5/22/01 ▪ MRI indeterminate ▪ Mammogram obtained on 11/28/01 determined implant intact ▪ Second MRI obtained 6/17/02 ▪ MRI indicated no evidence of rupture

CORE STUDY - AUGMENTATION

Confirmed Implant Non-Ruptures (False Reports) - Updated Data

There were no confirmed implant non-ruptures identified after PMA submission among Augmentation patients.

CORE STUDY - RECONSTRUCTION

Confirmed Implant Non-Ruptures (False Reports) - Updated Data

There were no confirmed implant non-ruptures identified after PMA submission among Reconstruction patients.

Core Study
Confirmed/Unconfirmed Ruptures by Implant Style

Implant styles	Augmentation		Reconstruction		Revision		Total Ruptures By Style	
	# of Ruptures	% of Total Devices Enrolled (N)	# of Ruptures	% of Total Devices Enrolled (N)	# of Ruptures	% of Total Devices Enrolled (N)	# of Ruptures	% of Total Devices Enrolled (N)
style 40	2*	0.5%(420)	0	0.0%(43)	0	0.0%(136)	2	0.3%(599)
style 45	0	0.0%(120)	0	0.0%(5)	2***	6.3%(32)	2	1.3%(157)
style 110	1*	0.4%(244)	1	1.5%(65)	2*	2.0%(104)	4	1.0%(413)
style 120	1*	0.8%(128)	0	0.0%(15)	0	0.0%(35)	1	0.6%(178)
style 153	1	1.3%(75)	12**	5.1%(234)	4	3.2%(125)	17	3.9%(434)
Total Confirmed/ Unconfirmed ruptures	5	0.5%(987)	13	3.6%(362)	8	1.9%(432)	26	1.5%(1781)

*1 is unconfirmed
**5 are unconfirmed
***2 are unconfirmed

CORE STUDY - AUGMENTATION

Table 171: Risk of First Occurrence of Implant Replacement/Removal

Time	By Patient				By Implant				
	Number Affected		Number Remaining		Number Affected		Number Remaining		Cumulative Risk % (95% CI)
	n	%	n	%	n	%	n	%	
4 Weeks	0	0.0%	482	0.0%	0	0.0%	963	0.0%	--
6 Months	4	0.8%	477	0.8%	7	0.7%	954	0.7%	(0.2%, 1.3%)
1 Year	13	2.7%	464	2.7%	24	2.5%	929	2.5%	(1.5%, 3.5%)
2 Years	22	4.7%	435	4.7%	41	4.3%	868	4.3%	(3.0%, 5.6%)
3 Years	32	7.5%	309	7.5%	60	7.0%	621	7.0%	(5.3%, 8.8%)

CORE STUDY - AUGMENTATION

Table 173: Risk of First Occurrence of Implant Removal without Replacement

Time	By Patient			By Implant		
	Number Affected	Number Remaining	Cumulative Risk % (95% CI)	Number Affected	Number Remaining	Cumulative Risk % (95% CI)
4 Weeks	0	482	0.0%	0	963	0.0%
6 Months	0	474	0.0%	0	948	0.0%
1 Year	0	462	0.0%	0	925	0.0%
2 Years	1	433	0.2% (0.0%, 0.7%)	2	868	0.2% (0.0%, 0.5%)
3 Years	5	309	1.5% (0.2%, 2.7%)	9	621	1.5% (0.4%, 2.1%)

CORE STUDY - AUGMENTATION

Table 173A: Distribution of Resolution Status of Primary Reason for Implant Removal/Replacement

Resolution Status	By Patient	
	n	%(N = 60)
Not Yet Resolved		
Undergoing Treatment	28	46.7%
Treatment Not Possible	0	0.0%
Refused Treatment	0	0.0%
<u>Total</u>	<u>28</u>	<u>46.7%</u>
Resolved		
With Reoperation and Explantation*	32	53.3%
With Reoperation Without Explantation	0	0.0%
With Non-surgical Treatment	0	0.0%
Without Treatment	0	0.0%
<u>Total</u>	<u>32</u>	<u>53.3%</u>

* Includes biopsy (n=0), size change (n=12), media anxiety (n=4) or unknown (n=0). Reoperations performed for these reasons do not require physicians to fill out a corresponding complication form, which documents the resolution status. Therefore, we assume they are resolved after reoperation, either with or without explantation.

CORE STUDY - AUGMENTATION

Table 175: Physician Evaluation of Explanted Devices

Characteristic	Ruptured Implants (n = 2)		Intact (Non-Ruptured) Implants (n = 58)	
	Yes (%)	No (%)	Yes (%)	No (%)
Capsule Torn*	0 (0.0%)	2 (100.0%)	0 (0.0%)	58 (100.0%)
Extracapsular Gel	0 (0.0%)	2 (100.0%)	0 (0.0%)	58 (100.0%)
Gel on Implant Surface	2 (100.0%)	0 (0.0%)	0 (0.0%)	58 (100.0%)
Removal Difficult	0 (0.0%)	2 (100.0%)	2 (3.4%)	56 (96.6%)

* Capsule not intact

Sent: Sunday, August 10, 2003 3:08 PM

CORE STUDY - AUGMENTATION

Appendix G: 3-Year Complication Rates for Augmentation Patients in Core Study and 1995 Saline Study

Complication	Core 3-Year Risk By Patient	A95 3-Year Risk By Patient
Swelling	23.3% (19.5%, 27.0%)	N/A
Reoperation	20.6% (16.8%, 24.4%)	21.1% (18.4%, 23.8%)
Bruising	9.3% (6.7%, 11.9%)	N/A
Capsular Contracture	8.3% (5.8%, 10.9%)	8.7% (6.8%, 10.6%)
Hypertrophic/Abnormal Scarring	8.1% (5.7%, 10.6%)	6.4% (4.8%, 8.0%)
Implant Replacement/Removal	7.5% (5.0%, 10.0%)	7.6% (5.8%, 9.4%)
Breast Pain	6.2% (4.0%, 8.4%)	15.6% (13.2%, 17.9%)
Ptosis	3.3% (1.7%, 5.0%)	N/A
Skin Rash	3.1% (1.6%, 4.6%)	1.6% (0.8%, 2.4%)
Implant Malposition	3.1% (1.5%, 4.8%)	8.2% (6.3%, 10.0%)
Loss of Nipple Sensation	3.1% (1.6%, 4.7%)	8.4% (6.5%, 10.2%)
Asymmetry	2.8% (1.3%, 4.4%)	10.1% (8.1%, 12.1%)
Other Nipple Related Observation	2.8% (1.3%, 4.2%)	N/A
Seroma/Fluid Accumulation	2.7% (1.3%, 4.1%)	2.6% (1.6%, 3.7%)
Redness	2.6% (1.1%, 4.1%)	N/A
Implant Rupture/Deflation	1.2% (0.1%, 2.2%)	5.0% (3.5%, 6.4%)
Loss of Skin Sensation	1.2% (0.3%, 2.2%)	N/A
Delayed Wound Healing	1.1% (0.1%, 2.1%)	0.7% (0.1%, 1.2%)
Infection	1.0% (0.1%, 1.9%)	0.7% (0.1%, 1.2%)
Hematoma	1.0% (0.1%, 1.9%)	1.6% (0.7%, 2.4%)
Wrinkling/Rippling	0.7% (0.0%, 1.6%)	10.5% (8.4%, 12.6%)
Implant Palpability/Visibility	0.6% (0.0%, 1.3%)	9.2% (7.2%, 11.1%)
Lymphadenopathy	0.4% (0.0%, 1.0%)	0.5% (0.0%, 1.0%)
Nipple Hypersensitivity	0.4% (0.0%, 1.0%)	N/A
Nipple Paresthesia	0.4% (0.0%, 1.0%)	9.3% (7.4%, 11.2%)
Skin Paresthesia	0.4% (0.0%, 1.0%)	7.2% (5.5%, 9.0%)
Other Complications	0.2% (0.0%, 0.6%)	2.3% (1.3%, 3.3%)
Implant Extrusion	0.2% (0.0%, 0.6%)	0.1% (0.0%, 0.4%)
Capsule Calcification	0.2% (0.0%, 0.7%)	1.2% (0.4%, 1.9%)
Tissue or Skin Necrosis	0.2% (0.0%, 0.6%)	0.7% (0.1%, 1.2%)
Lymphedema	0.2% (0.0%, 0.6%)	N/A
Irritation	0.0% --	2.9% (1.8%, 4.0%)
Pneumothorax	0.0% --	0.1% (0.0%, 0.3%)
Skin Hypersensitivity	0.0% --	N/A

CORE STUDY - SERIAL MRI

Table 7: Risk of First Occurrence of Silent Rupture

Time	By Patient			By Implant		
	Number Affected	Number Remaining	Cumulative Risk % (95% CI)	Number Affected	Number Remaining	Cumulative Risk % (95% CI)
4 Weeks		N/A		0	597	0.0%
6 Months		N/A		0	597	0.0%
1 Year		N/A		0	597	0.0%
2 Years		N/A		14	554	2.4% (1.2%, 3.6%)
3 Years		N/A		15	267	2.7% (1.3%, 4.0%)

SERIAL MRI

Table 7A: Risk of First Occurrence of Silent Rupture

Time	By Patient				By Implant			
	Number Affected		Number Remaining		Number Affected		Number Remaining	
	n	% (95% CI)	n	% (95% CI)	n	% (95% CI)	n	% (95% CI)
1 Year	.	(., .)	.	(., .)	0	0.0%	597	0.0%
2 Years	.	(., .)	.	(., .)	14	2.4%	554	2.4% (1.2%, 3.6%)
3 Years	.	(., .)	.	(., .)	15	2.7%	267	2.7% (1.3%, 4.0%)

SERIAL MRI

Table 7B: Risk of First Occurrence of Silent Rupture: Subset Cohort Augmentation

Time	By Patient				By Implant			
	Number Affected		Number Remaining		Number Affected		Number Remaining	
	n	% (95% CI)	n	% (95% CI)	n	% (95% CI)	n	% (95% CI)
1 Year	.	(. , .)	.	(. , .)	0	0.0%	289	0.0%
2 Years	.	(. , .)	.	(. , .)	2	0.7% (0.0%, 1.6%)	260	0.7% (0.0%, 1.6%)
3 Years	.	(. , .)	.	(. , .)	3	1.2% (0.0%, 2.6%)	176	1.2% (0.0%, 2.6%)

SERIAL MRI

Table 7C: Risk of First Occurrence of Silent Rupture: Subset Cohort Reconstruction

Time	By Patient				By Implant			
	Number		Cumulative		Number		Cumulative	
	Affected	Remaining	Number	Risk	Affected	Remaining	Risk	
1 Year	n	n	%	(95% CI)	n	n	%	(95% CI)
2 Years	.	.	·	(% , .)	0	170	0.0%	--
3 Years	.	.	·	(% , .)	8	160	4.7%	(1.5%, 7.9%)
	.	.	·	(% , .)	8	24	4.7%	(1.5%, 7.9%)

SERIAL MRI

Table 7D: Risk of First Occurrence of Silent Rupture: Subset Cohort Revision

Time	By Patient				By Implant			
	Number Affected	Number Remaining	Cumulative Risk		Number Affected	Number Remaining	Cumulative Risk	
	n	n	% (95% CI)		n	n	% (95% CI)	
1 Year	.	.	. (., .)	.	0	138	0.0%	0.0%
2 Years	.	.	. (., .)	.	4	134	2.9%	(0.1%, 5.7%)
3 Years	.	.	. (., .)	.	4	67	2.9%	(0.1%, 5.7%)

CORE STUDY - SERIAL MRI

Table 2B: Number of Patients/Implants with MRIs

	Patients				Implants			
	Aug	Recon	Revis	Total	Aug	Recon	Revis	Total
No MRIs	21	7	5	33	42	14	10	66
At Least One MRI	145	101	72	318	289	170	138	597
Total	166	108	77	351	331	184	148	663

Breakdown of At Least One MRI

	Patients				Implants			
	Aug	Recon	Revis	Total	Aug	Recon	Revis	Total
1 MRI	62	99	71	232	123	168	136	427
2 MRIs	83	2	1	86	166	2	2	170
Total Number of MRIs*	228	103	73	490	455	172	140	767

*Total number of MRIs is calculated as: (number with 1 MRI * 1) + (number with 2 MRIs * 2)

Sent: Monday, September 01, 2003 4:08 AM

Connective Tissue Disease (CTD) Signs/Symptoms

Methods

As suggested in FDA's Guidance Document, *Guidance for Saline, Silicone Gel, and Alternative Breast Implants; Final Guidance for Industry*, Inamed collected four types of CTD data: rheumatic diseases, rheumatic syndromes, rheumatic signs/symptoms, and other signs/symptoms. This information was collected by asking patients to complete an *Activities and Lifestyle* questionnaire prior to receiving their breast implants and at 1- and 2-years post-implantation. (As the study progresses, the questionnaire is also scheduled to be collected at 4, 6, 8, and 10 years post-implantation.) Investigators reviewed each patient's completed questionnaire for signs/symptoms of a possible CTD. If a CTD was suspected the investigator referred the patient to a rheumatologist, if necessary, for further evaluation. If a patient was referred to a rheumatologist and the referral confirmed that the patient had a CTD, a *CTD Confirmation Form* (CRF Form 11) was completed and returned to Inamed's Clinical Research Department.

Rheumatic disease and rheumatic syndrome information was collected on *the CTD Confirmation Form* and was reported in the original PMA, submitted December 27, 2002, in *RESULTS, Section D. Pre- Vs. Post-Implant Medical History, 3. Connective Tissue/Autoimmune Disease*, and also in Tables 189-190 (Attachments 7, 8 and 9 for the Augmentation, Reconstruction and Revision cohorts, respectively). Updated information was presented in Tables 189-190 of Attachments 2, 3 and 4 of PMA P020056, Amendment 3, submitted June 12, 2003, with subsequent additional information submitted via email upon various FDA requests.

Rheumatic signs/symptoms and other signs/symptoms, although collected on the *Activities and Lifestyle* questionnaire, were not analyzed/reported in the original PMA in 2002 because it was not intended for these data to be statistically analyzed. Instead, as discussed above, the intention was for the investigator to review the completed questionnaire and use it as a basis for referring patients to a rheumatologist if necessary. Furthermore, based on a February 17, 1998 memorandum from Dr. Sahar Dawisha to Dr. Celia Witten, Dr. Dawisha indicated that, "The purpose of this screening is primarily to document rheumatic signs and symptoms at baseline and at follow-up. FDA recognizes that the utilization of these data for the purposes of determining causality or association of breast implants and CTD is not valid due to insufficient sample sizes for appropriate statistical power. Therefore, these data will be interpreted in a qualitative context to obtain information on pre-implantation CTD signs and symptoms." Dr. Dawisha went on to state, "FDA recognizes that there currently are few validated CTD screening instruments currently available, making quantitatively statistical conclusions problematic. However, despite this limitation, FDA believes that these data will be of value in documenting rheumatic signs and symptoms and in determining CTD diagnoses, if present."

At the request of Dr. Sahar Dawisha in August, 2003, and in consultation with Dr.

specific signs/symptoms collected on the *Activities and Lifestyle* questionnaire before and after implantation with Inamed's gel-filled breast implants were analyzed. The following data was examined using pre-implantation and 2-year data:

- disability index (MHAQ)
- signs/symptom categories
 - skin
 - muscle
 - joint
 - neurological
 - gastrointestinal
 - urinary
 - general
 - other

Although in August, 2003, Dr. Dawisha requested a Kaplan Meier analysis consistent with FDA's guidance document, a comparison of the prevalence of signs/symptoms at baseline to the prevalence at 2-years was determined to be more appropriate than a Kaplan Meier analysis. This analysis plan was chosen in consultation with Dr. and allows a comparison by using each patient as her own control. Inamed believes that not only is the chosen analysis more informative, but it also allows Inamed to maintain a consistent approach for analysis of patient questionnaire data vs. physician reported data. This type of analysis is similar to the pre vs. post comparison analysis that Inamed performs with the quality of life patient questionnaire data. For the Core breast implant study Inamed has only performed Kaplan Meier analyses with physician reported data on local complications.

Disability Index

Each patient's disability index was calculated using items A-H in Question 1 on the *Activities and Lifestyle* CRF. The Modified Health Assessment Questionnaire (MHAQ) was developed by Dr. [redacted] and his colleagues using 8 of the 20 HAQ (Health Assessment Questionnaire) disability items^{1,2,3,4}, and has been shown to be significantly correlated with the HAQ scores.¹ The MHAQ score was calculated by taking the average of the 8 responses; possible scores ranged from 1 "Without ANY Difficulty" to 4 "UNABLE to Do". Change scores were calculated by subtracting the pre-implantation disability score from the post-implantation score. The non-parametric Sign test was used to compare if change scores were significantly different than zero between pre-implantation and 2 years post-implantation. P-values from the sign test were reported. A paired t-test was not used because the data were not normally distributed. Furthermore, under the direction of Dr. [redacted] published mean MHAQ scores from a population of patients with Rheumatoid Arthritis, Fibromyalgia, or Scleroderma are reported for a qualitative comparison with the mean scores found in the Core breast implant populations.

Signs/Symptoms Categories

Each patient was asked to indicate if they experienced any of the 72 signs/symptoms listed in Question 13 of the *Activities and Lifestyle* CRF by marking check boxes next to the listed signs/symptoms. These symptoms were then grouped into the categories suggested by FDA's breast implant guidance document, plus 3 additional categories (Gastrointestinal, Urinary, and Other). The signs/symptoms included in each category are described below. If a specific sign/symptom was suggested in the guidance and not collected using the same syntax it is noted parenthetically in each category as "collected as ...".

¹ Pincus T, Summey JA, Soraci SA, Jr., Wallston KA, Hummon NP. Assessment of patient satisfaction in activities of daily living using a modified Stanford health assessment questionnaire. *Arthritis Rheum* 1983; 26:1346-1353.

² Pincus T, Callahan LF, Brooks RH, Fuchs HA, Olsen NJ, Kaye JJ. Self-report questionnaire scores in rheumatoid arthritis compared with traditional physical, radiographic, and laboratory measures. *Ann Intern Med* 1989; 110:259-266.

³ Pincus T, Brooks RH, Callahan LF. Prediction of long-term mortality in patients with rheumatoid arthritis according to simple questionnaire and joint count measures. *Ann Intern Med* 1994; 120:26-34.

⁴ Pincus T, Swearingen C, Wolfe F. Toward a multidimensional health assessment questionnaire (MDHAQ): Assessment of advanced activities of daily living and psychological status in the patient friendly health assessment questionnaire format. *Arthritis Rheum* 1999; 42:2220-2230.

- Skin Category
 - alopecia (collected as “loss of hair”), facial rash (collected as “skin rash” and “swelling of face”), ecchymosis, purpura, telangiectasia and petechiae (all collected as “unusual bruising” and “unusual bleeding”), urticaria (collected as “hives”), other skin problems
- Muscle Category
 - muscle weakness, paralysis of arms/legs, myalgias (collected as “muscle pain/aches/cramps”), back pain, neck pain
- Joint Category
 - arthralgia & arthritis (collected as “joint pain”, “swelling of hands”, “swelling of other joints”), morning stiffness⁵
- Neurological Category
 - memory problems, cognitive dysfunction (collected as “problems with thinking” and “headaches”), paresthesia (collected as “numbness/tingling of arms/legs”), dizziness (collected as “losing your balance”), ringing in the ears
- Gastrointestinal Category
 - heartburn, stomach pain/cramps, nausea, vomiting, constipation, diarrhea, dark stool, blood in stool, loss of appetite, gastrointestinal trouble (collected in Question #3)⁶
- Urinary Category
 - urinating too often, problems with urination
- General Category
 - fever, swollen glands, weight gain/loss, fatigue (collected in Questions #4 and #13)⁶, generalized pain (collected in Question #2)⁶
- Other Category
 - dry eyes, other eye problems, sores in mouth, dry mouth, problems with taste, trouble swallowing

The following items were collected in Question 13, but were not included in any of the categories because they are not directly applicable to the categories above: swelling of ankles, problems with hearing, stuffy nose, problems with smell, cough, shortness of breath, pain in chest, wheezing, heart pounding, abnormal vaginal bleeding, gynecological problems, any new health problem, any new drug prescription, any discontinued drug, side effects of drugs, smoking cigarettes, more than 2 alcoholic drinks/day, depression – feeling blue, anxiety, problems with sleeping, sexual problems, change in marital status/address/job/duties of job, quit working/retired, applied for disability, and problems with social activities.

⁵ Morning stiffness is collected in Question 9 on the Activities and Lifestyle CRF. Although it is not included in Question 13, it is included in the Joint category because “morning stiffness” was specifically requested in FDA’s guidance.

⁶ Questions 2, 3, and 4 on the Activities and Lifestyle CRF contain visual analog scales to measure Pain, GI Trouble and Fatigue, respectively. These visual analog scores were transformed to a scale ranging from 0-10 with 10 being the worst/most pain or fatigue. Under Dr. direction, a score of ≥ 3 indicated a severity that should be included in the applicable category.

For each sign/symptom category, the percentage of patients with prevalent signs was computed pre and post-implantation and reported with the p-value results from a McNemar test. Chi-square testing was not employed because it requires two independent datasets; the data obtained preoperatively is not independent of the postoperative data because each group contains the same patients. Furthermore, the prevalence of individual signs within each significant category was presented.

Results & Conclusions

A total of 773 patients completed an *Activities and Lifestyle* CRF between 1.5 and 2.5 years.

- 423 Augmentation with a mean age of 35 years (18-60 years)
- 178 Reconstruction with a mean age of 50 years (29-83 years)
- 172 Revision with a mean age of 44 years (23-79 years)

Table 1 shows the results of the MHAQ analysis. All comparisons were non-significant. Furthermore, Pincus et al.⁴ report mean MHAQ scores for various populations of patients: Rheumatoid Arthritis 1.73, Fibromyalgia 1.64, and Scleroderma 1.48. All mean scores from the Augmentation, Reconstruction, and Revision cohorts (as reported in Table 1) are lower than those reported by

Table 2 shows the results of the signs/symptoms analysis. All comparisons were non-significant, except for comparisons in 3 categories. In the Muscle category, signs/symptoms significantly increased in the Augmentation cohort from 19.4% to 28.0%. In the Joint category, signs/symptoms significantly increased in the Augmentation and Reconstruction cohorts from 13.0% to 22.0% and from 42.6% to 58.0%, respectively. Finally, in the General category, signs/symptoms significantly increased in the Augmentation cohort from 15.5% to 25.6%.

Table 3 shows the results of the individual signs/symptoms analysis for the categories with significant results in Table 2. Within the muscle category, “muscle weakness” significantly increased post-implantation in the Augmentation cohort. Within the joint category, “joint pain” and “morning stiffness” significantly increased post-implantation in the Augmentation cohort, and “joint pain” alone significantly increased post-implantation in the Reconstruction cohort. Within the General category in the Augmentation cohort, both measures of fatigue significantly increased post-implantation. However, the number of patients who reported fatigue using both measures pre-implantation is inconsistent. Twenty-seven patients reported unusual fatigue pre-implantation “in the past week” via Question #4, but only six patients reported unusual fatigue pre-implantation “over the last month” via Question #13.

In conclusion, although statistically significant increases over baseline occurred in three categories, there is no clinical evidence to indicate that these patients have developed or are developing CTD. In fact, there was only one diagnosis each of Rheumatoid Arthritis (RA), systemic sclerosis/scleroderma and Fibromyalgia identified in the Core study. The patient reported to have RA was subsequently identified to have a negative RA factor, and therefore the RA diagnosis was not confirmed, leaving only two confirmed diagnoses of CTD. Furthermore, it is important to reiterate that these results should be interpreted carefully because the questionnaire was not designed to diagnose CTD, but instead was designed to document symptoms for investigators to review and use as a tool to help them determine if further rheumatological work-up is warranted. This study was not designed to test a casual relationship between gel-filled breast implants and CTD. It is well recognized that the patient population for which breast implants are indicated are susceptible to the development of CTD irrespective of whether they undergo breast implantation.

Table 1: Mean MHAQ Scores Pre vs. Post Implantation

<i>Cohort</i>	N	Type	Mean	std	p-value*
Augmentation	451	Pre	1.005	0.051	.
	423	Post	1.008	0.045	.
	385	Change	0.002	0.068	0.1306
Reconstruction	200	Pre	1.038	0.113	.
	177	Post	1.032	0.094	.
	161	Change	-0.008	0.142	0.5074
Revision	203	Pre	1.015	0.077	.
	172	Post	1.049	0.194	.
	157	Change	0.030	0.157	0.0180

* significant p-value at the 0.017 level (since 3 tests are performed alpha is adjusted using bonferonni correction 0.05/3)

Table 2: Frequency Comparison

<i>Category/Cohort</i>	Pre-Implant Signs/Symptoms n (%)	Post-Implant Signs/Symptoms n (%)	p-value*
<i>Skin</i>			
Augmentation	29 (7.5%)	50 (13.0%)	0.00549
Reconstruction	20 (12.3%)	35 (21.6%)	0.02753
Revision	13 (8.3%)	24 (15.3%)	0.08953
<i>Muscle</i>			
Augmentation	75 (19.4%)	108 (28.0%)	0.00133*
Reconstruction	56 (34.6%)	65 (40.1%)	0.22205
Revision	46 (29.3%)	62 (39.5%)	0.02590
<i>Joint</i>			
Augmentation	50 (13.0%)	85 (22.0%)	0.00003*
Reconstruction	69 (42.6%)	94 (58.0%)	0.00126*
Revision	41 (26.1%)	56 (35.7%)	0.01353
<i>Neurological</i>			
Augmentation	158 (40.9%)	180 (46.6%)	0.04674
Reconstruction	78 (48.1%)	97 (59.9%)	0.00540
Revision	59 (37.6%)	78 (49.7%)	0.00661
<i>General</i>			
Augmentation	60 (15.5%)	99 (25.6%)	0.00021*
Reconstruction	56 (34.6%)	68 (42.0%)	0.13367
Revision	55 (35.0%)	66 (42.0%)	0.18485
<i>Other</i>			
Augmentation	52 (13.5%)	59 (15.3%)	0.47669
Reconstruction	37 (22.8%)	43 (26.5%)	0.42959
Revision	28 (17.8%)	34 (21.7%)	0.37709
<i>Gastrointestinal</i>			
Augmentation	101 (26.2%)	119 (30.8%)	0.12958
Reconstruction	66 (40.7%)	73 (45.1%)	0.44996
Revision	44 (28.0%)	56 (35.7%)	0.14801
<i>Urinary</i>			
Augmentation	3 (0.8%)	11 (2.8%)	0.03857
Reconstruction	9 (5.6%)	9 (5.6%)	1.00000
Revision	5 (3.2%)	13 (8.3%)	0.07681

* significant p-value at the 0.002 level (since 24 tests are performed alpha is adjusted using bonferonni correction 0.05/24)

Table 3: Frequency Comparison

<i>Category/(Sign/Symptom)</i>	Pre-Implant Signs/Symptoms n (%)		Post-Implant Signs/Symptoms n (%)		p-value*
<i>Muscle - Augmentation</i>					
Muscle Weakness	0	(0.0%)	12	(3.1%)	0.00049*
Paralysis of Arms/Legs	0	(0.0%)	0	(0.0%)	--
Muscle Pain/Aches/Cramps	34	(8.8%)	57	(14.8%)	0.00674
Back Pain	61	(15.8%)	78	(20.2%)	0.04980
Neck Pain	39	(10.1%)	58	(15.0%)	0.00432
<i>Joint - Augmentation</i>					
Joint Pain	10	(2.6%)	26	(6.7%)	0.00249*
Swelling of Hands	5	(1.3%)	10	(2.6%)	0.17969
Swelling of Other Joints	0	(0.0%)	6	(1.6%)	--
Morning Stiffness	39	(10.1%)	70	(18.1%)	0.00012*
<i>Joint - Reconstruction</i>					
Joint Pain	17	(10.5%)	31	(19.1%)	0.00936
Swelling of Hands	10	(6.2%)	15	(9.3%)	0.35928
Swelling of Other Joints	3	(1.9%)	5	(3.1%)	0.72656
Morning Stiffness	57	(35.2%)	84	(51.9%)	0.00020*
<i>General - Augmentation</i>					
Fever	15	(3.9%)	17	(4.4%)	0.84502
Swollen Glands	6	(1.6%)	13	(3.4%)	0.11847
Weight Gain	7	(1.8%)	17	(4.4%)	0.03088
Weight Loss	9	(2.3%)	4	(1.0%)	0.17969
Fatigue (Q#4)	27	(7.0%)	58	(15.0%)	0.00007*
Fatigue (Q#13)	6	(1.6%)	43	(11.1%)	< 0.00001*
Pain	8	(2.1%)	19	(4.9%)	0.03469

* significant p-value at the 0.0025 level (since 20 tests are performed alpha is adjusted using bonferonni correction 0.05/20)