



Breast Implants: A Research and Regulatory Summary

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More women are getting breast implants than ever before. In 2004, more than 330,000 women and teenagers underwent breast implant surgery for augmentation¹ and approximately 35,000 women underwent breast implant surgery for reconstruction after mastectomy.² The number of breast augmentations of women and teenagers has more than tripled since 1997, when it was 101,176.³

However, the dramatic increase in breast implant surgery does not necessarily reflect a similarly dramatic increase in the number of women with breast implants. Many women who undergo surgery are replacing old implants that have broken or caused problems; some women report as many as ten or more surgeries as their implants are replaced over the years. There are no available statistics on how many women undergo their first breast implant surgery every year.

Debate swirls over the risks of breast implants, and physicians and patients are justifiably confused by the conflicting information available. This summary provides information about what is known and not known about the risks of breast implants.

The Role of the Food and Drug Administration (FDA) in Safety Research

Breast implants were first sold in the 1960's, but the FDA did not have the authority to regulate them until 1976. Sales were relatively slow until the 1980's but by 1990, almost one million women had breast implants, even though there were no published studies about their safety, and the FDA had never approved them. Finally, in 1991, the FDA required the manufacturers of silicone gel breast implants to submit safety studies. Unfortunately, these studies were inadequate; for example, in the McGhan prospective study, only 35% of the patients had been followed for at least three months, and there were only three reconstruction patients.⁴ Because of the lack of clinical data, silicone implants were not approved. Instead, the FDA approved a compassionate need exemption policy on October 23, 1992, which allowed silicone implants to remain available, primarily to reconstruction patients and women who already had breast implants that they wanted replaced. Meanwhile, articles questioning the health risks of breast implants were being published in medical journals.

Under the FDA's compassionate need exemption policy, silicone gel implants remain restricted in the U.S. to clinical trials, including a large "adjunct study" for reconstruction patients and women with broken implants. Smaller numbers of first-time augmentation, reconstruction, and implant replacement patients are in each company's "core study." It is important to note that the definition of reconstruction patients includes many women who are not mastectomy patients; women can also be "reconstructed" after "deformities" such as very droopy breasts and "severe" asymmetry (both subjectively defined by the plastic surgeons). In addition, women who are unhappy with their saline breast implants are often able to find a physician who will enroll them in the adjunct study of silicone gel implants. However, all women who have had surgery with silicone gel implants since 1992 have been required to be informed that the implants are not approved by the FDA, to provide informed consent, and to be regularly evaluated by their plastic surgeons as part of the study. Implant manufacturers could have collected and published extensive safety data from these studies. However, they have not done so.

Major shortcomings have been reported regarding the adjunct studies and core studies, in terms of entry criteria, data collection, and patients' informed consent. Numerous patients have informed our Center and testified before the FDA that plastic surgeons enrolled them in these clinical trials for non-existing deformities, or did not obtain informed consent. Many patients report that their physicians encouraged them to enroll in the study as a way to qualify for silicone implants, explaining that they could immediately drop out. That anecdotal claim is supported by the enormous loss to follow-up; Inamed data discussed at the FDA's October 2003 Advisory Panel meeting indicates that only 27% of the reconstruction patients and 20% of the revision patients

were followed for three years. As a result of this very low follow-up rate, these "studies" do not provide meaningful safety data.

The October 2003 FDA Advisory Panel meeting was held to consider approval of silicone breast implants made by Inamed. After considering the Advisory Panel recommendations and the scientific data, the FDA decided not to approve Inamed silicone breast implants in January 2004. At the same time that the decision was announced, the FDA issued a new guidance specifying the type of research needed to obtain approval of any breast implants in the future. A major focus of the guidance document is for manufacturers to determine why implants break, how long they last, and the health consequences of broken and leaking breast implants. On April 11-13, 2005, the FDA will hold an advisory panel meeting to consider the research on silicone breast implants that has subsequently been submitted by two companies, Inamed and Mentor.

Types of Breast Implants

The 40-year history of silicone breast implants is a history of trying to reduce complications, especially common problems such as breast hardness and pain caused by capsular contracture. Although breast implants were not studied in clinical trials for the first 25 years, clinical experience indicated that design modifications seemed to improve the outcome at first, but were later found to be ineffective at fixing the problems and often caused new ones. For example, since the mid-1960's implant modifications have included adding a Dacron patch, removing the Dacron patch, changing the thick gel to a thinner gel, changing the thinner gel to a thicker gel, making the silicone shell textured, covering the shell with polyurethane foam, removing the foam when it was found to break down to a carcinogen, making the shell smooth, changing the shape of the implants, and reducing "silicone

bleed.” All of these changes were “studied” informally when patients underwent surgery, rather than in clinical trials. A Congressional report summarizing these changes referred to the patients as guinea pigs.⁴

The silicone gel breast implants being reviewed by the FDA in April 2005 are essentially identical to those made in the early 1990’s. Inamed’s Senior Director of Regulatory and Clinical Affairs testified to the FDA that “it is basically the same product it was 10 years ago...it is essentially the same product.”⁵

In addition to changes in silicone gel breast implants, implant makers have tried to improve the product by using fewer materials other than silicone gel. Saline breast implants have a silicone envelope and are filled with salt water. Saline breast implants have been available for decades, but it was not until May 2000 that the FDA approved saline implants for the first time. Before approving these devices, the FDA required 3-year studies of local complications, such as pain, infection, hardening, and the need for additional surgery. They did not require studies of other health problems. In addition to saline, three other kinds of implants were available in recent years, primarily outside the United States: Trilucent implants (with soybean oil filler), and Novagold and PIP hydrogel implants, which were filled with a plastic gel. Although never approved as safe in the U.S., these implants were vigorously promoted by plastic surgeons and the media as a “natural” and safer alternative to silicone or saline implants. Clinical trials, however, were apparently never conducted on humans with these implants, and all were removed from the market in 2000 because of safety concerns.^{6, 7, 8, 9} Their removal from the market, after being enthusiastically praised by doctors and patients, serves as a reminder that the long-term risks of implants are not always obvious during the first few years of use.

Frequency of Local Complications

Risks associated with surgery include infection, hematoma (blood or tissue fluid collecting around an implant), and the risks associated with anesthesia.

Pain and Capsular Contracture: All implants are “foreign bodies,” and a woman’s body reacts by forming a capsule of scar tissue around the implants that can become too tight for the implant. This common problem is called **capsular contracture**. When that occurs, the breasts can become very hard, misshapen, and cause mild discomfort or severe, chronic pain. Research submitted in support of Inamed’s 2003 application showed severe capsular contracture occurring in 16% of reconstruction patients and 8% of augmentation patients within 3 years.

Comparing Inamed data on saline breast implants and silicone gel breast implants shows many of the same types of complications; however, complication rates from silicone implants tend to be higher.^{10, 11} For example, 46% of silicone gel reconstruction patients and 21% of saline reconstruction patients underwent at least one re-operation within three years, 25% of silicone patients and 8% of saline patients had implants removed, and 6% of silicone patients and 16% of saline patients had breast pain. Complication rates were lower but still substantial for augmentation patients.

A study of Danish women who had breast implants for an average of 19 years found that women with implants were almost three times as likely to report breast pain compared to breast reduction patients; the question was not asked of women in a control group since it was assumed they did not experience breast pain.¹² In addition, two-thirds of the women with implants reported moderate or severe breast hardness.

There are other well-documented local com-

plications that can result from breast implants. For example, some women lose sensitivity in their breasts, and others become overly sensitive; these problems can interfere with sexual intimacy. The cosmetic outcome is sometimes disappointing, with breasts looking or feeling unnatural or asymmetrical.

Rupture: All breast implants will eventually break. When silicone gel breast implants break, there are often no symptoms, so accurate estimates of rupture rates depend on magnetic resonance imaging (MRIs). Patients who testified before the FDA and clinical evidence indicates that some breast implants break during the first few weeks or months, while others last more than 15 years. In a study conducted by researchers at the FDA, most women had at least one broken implant within 10 years, and the likelihood of rupture increased over time.¹³ The women in the FDA study had not had their implants removed, did not know that their implants were broken, and were not seeking help because of implant concerns. Despite the fact that these women were “satisfied customers” rather than women seeking medical care, MRIs found that silicone had migrated outside of the breast capsule for 21% of the women in the study. Most of the women were unaware that this had happened. Inamed’s study of their silicone gel implants found that between 1 - 6% break within three years.¹¹ A Danish study of ruptured silicone gel implants reported that most lasted for ten years; however, by the time the women in that study had implants for 15 years or more, a substantial percentage of the implants broke every year.¹⁴

Leakage: Numerous studies have shown silicone leakage into the scar capsules surrounding breast implants, even for implants that are not ruptured. More worrisome, researchers at Case Western Reserve and the Armed Forces Institute of Pathology have reported finding silicone in the lymph

nodes of women with breast implants, which can then migrate to other organs.^{15,16} Silicone in the lymph nodes can only be removed by removing the lymph nodes; silicone in organs such as the lungs, liver, and brain cannot be removed. The health risks associated with migrated silicone are unknown; however, case reports have indicated fatalities and serious health risks when liquid silicone injected in the breasts migrated to the lungs or other organs. Although silicone implants are filled with gel rather than the liquid form of silicone, the implants sometimes leak a silicone liquid or thin gel.

A study published by the Royal Academy of Medicine in Scotland found that a woman with a broken silicone gel implant in her calf was coughing up silicone identical to the kind in her implant.¹⁷ This has potentially serious implications for women with leaking breast implants, since silicone gel breast implants are considerably larger and closer to the lungs than calf implants.

Mammography: Breast implants interfere with the detection of breast cancer because implants can obscure the mammography image of a tumor. Implants therefore have the potential to delay the diagnosis of breast cancer. Although special techniques are designed to minimize the interference of the implants, the most recent research indicates that 55% of breast tissue and tumors will still be obscured. That is much higher than the 33% obscured in women without implants in the same study.¹⁸ Mammograms tend to be less accurate if the woman has capsular contracture. In addition, women with implants may be reluctant to undergo mammograms because of fear of rupture, and a study by FDA scientists indicates that silicone or saline implants sometimes rupture when women undergo mammograms.¹⁹ There is no research evidence that implants cause breast cancer, and research findings on whether there is a delay in diagnosis have been inconsistent. A delay in diagno-

sis could have serious health implications, and decrease women's options for breast-conserving surgery, and such delays have been reported by patients.¹⁹

Breastfeeding: According to the Institute of Medicine (IOM), women with any kind of breast surgery, including breast implant surgery, are up to three times more likely to have an inadequate milk supply for breastfeeding.²⁰ Concerns about the chemicals from the implants passing to infants through breastfeeding have also been raised, but there is insufficient research information available. However, a study presented at the American Chemical Society's 2004 August meeting found exceptionally high concentrations of platinum, a known potential toxin, not only in women with silicone breast implants, but also in the children they bore and breastfed.²¹ The American Academy of Pediatrics always encourages breastfeeding unless there is clear evidence of risk, whether from implants or any other exposure. However, they have not yet reviewed or formally commented on the aforementioned study.

Autoimmune and Connective Tissue Diseases

The greatest controversy regarding the risks of breast implants is whether they increase the risk of autoimmune disease and connective tissue disease. Studies from the 1990's tend to show no increase in risk, but more recent studies suggest an increased risk.

A study conducted by FDA scientists found a statistically significant link between implants and fibromyalgia and several connective tissue diseases.²² The study focused on women who had silicone breast implants for at least six years, and found that women with leaking silicone implants were significantly more likely to report a diagnosis of painful and debilitating diseases such as fibromyalgia, dermatomyositis, polymyositis, Hashimoto's thyroiditis, mixed connective tis-

sue disease, pulmonary fibrosis, eosinophilic fasciitis, and polymyalgia. The risk of fibromyalgia remained even after controlling for patient's age, implant age, and implant manufacturer. Extracapsular leakage was evaluated using an MRI.

A study by Aziz *et al* examined 95 women who had silicone gel-filled breast implants and rheumatologic symptoms. These researchers found that the symptoms improved in 42 (97%) of the 43 women who had their breast implants removed and not replaced.²³ In contrast, rheumatologic symptoms worsened in 50 (96%) of the 52 women who did not have their implants removed.

Scientists at the National Cancer Institute (NCI) found a statistically significant increase in reported connective tissue diseases among breast augmentation patients, but also found that many of the women made errors in their self-reported diagnoses.²⁴ For example, many women who reported having rheumatoid arthritis had osteoarthritis instead, according to their medical records. The NCI study included women who had breast implants for at least **seven years**. The findings suggest that there are increased symptoms among women with breast implants, but it is not clear if there is an increase in specific diagnoses. As a result, the researchers concluded that the associations between breast implants and arthritis, scleroderma, Sjogren's syndrome, and other connective tissue diseases need further study.

A study of Danish women who had breast implants for an average of 19 years found that they were significantly more likely to report fatigue, Raynaud-like symptoms (white fingers and toes when exposed to cold), and memory loss and other cognitive symptoms, compared to women of the same age in the general population.¹² Ten percent of the women with implants had already had their implants removed and not replaced,

which might have reduced these symptoms. Despite reporting that women with implants were between two and three times as likely to report those symptoms, the researchers concluded that long-term exposure to breast implants “does not appear to be associated with” autoimmune “symptoms or diseases.” The study was funded by Dow Corning. Prior to these recent studies, most published research that has focused on autoimmune or connective tissue diseases studied women who had implants for a relatively short time, ranging from a few months to a few years. The minimum exposure to breast implants was usually **one month**. These studies are the basis for a report on implants by the IOM, a report by Judge Pointer’s scientific panel, and a meta-analysis published in the *New England Journal of Medicine* regarding the lack of evidence that implants cause systemic disease.^{19, 25, 26} All three of these reports are based on the same 17-20 epidemiological studies that were published prior to 1999. Since many connective tissue and autoimmune diseases are relatively rare among young women and most take many years to develop and be diagnosed, these studies are not designed to answer questions about long-term safety. Their major flaws are as follows:

- ◆The case-control studies relied on women accurately telling a stranger whether they had breast implants, and most included very few women who admitted having breast implants. The accuracy of their responses was not verified.
- ◆The studies include substantial numbers of women who had implants for just a few months or years, and therefore do not have the statistical power to determine whether or not breast implants increase the long-term risks of getting these diseases.
- ◆The number of women in the studies who had breast implants for 10-15 years

or more is too small to conclusively evaluate an increased risk of disease.

- ◆Disease diagnoses were based on medical records or self-reports, not medical exams. Several studies had an even greater flaw: autoimmune disease was based on hospital records rather than medical diagnoses. Most women with autoimmune symptoms or diseases are not treated in hospitals.

Among the studies reviewed by the IOM, only one study, by Schusterman *et al*, includes a diagnosis based on a medical exam, and all the women in that study had implants for less than two years, which is too short a time to meaningfully evaluate disease risk.

In addition, several European studies that purported to show no increased risk of autoimmune diseases actually indicated an increased risk of neurological or autoimmune disease that was similar for women who had breast augmentation or breast reduction.^{27, 28} Using breast reduction patients as a comparison sample, the researchers reported that the augmentation patients were not significantly more at risk. However, the articles clearly stated that both groups had a higher proportion of women with these diseases than expected. Therefore, the interpretation of “no increased risk” was inappropriate; rather both types of breast surgery patients were apparently at increased risk.

These findings raise concerns about autoimmune disease that need to be answered with long-term studies. In addition, former FDA researchers have reported that silicone stimulates an immune response, and their cellular analyses indicate that these responses are associated with atypical forms of connective tissue disease.²⁹

In summary, research on connective tissue

and autoimmune diseases raises unanswered questions about long-term safety. Results are not conclusive because of relatively short-term follow-up and limitations of the outcome measures. Self-reports tend to show significant increases in health risks, whereas studies that rely on medical records and hospitalization are less likely to show significant increased risks. In industry-funded studies, even when studies indicate an increase in symptoms among women with implants, the authors sometimes conclude that there is no evidence of increased health problems. Overall, there is evidence of increased symptoms in several studies, and more research is needed to draw conclusions about the safety of implants in terms of systemic autoimmune disease.

Cancer, Lung Disease, and Suicide

Implant manufacturers claim that there are dozens of long-term studies proving that implants are safe. Almost all of these “long-term” studies consist primarily of women who have had implants for a short period of time, ranging from one day to several years. Although the women may have implants for an average of 5 or 8 or even 10 years, the number of women with implants for more than 10 years is quite small. Epidemiologists estimate that 15-20 years of follow-up would be necessary for a well-designed study of cancer after exposure, whether to asbestos, tobacco, or breast implants. Most of these studies were funded by Dow Corning, conducted by a core group of researchers at a research institute that receives substantial funding from Dow Corning, and have been used to defend the company from liability.

There are very few published studies that have medically evaluated sufficient numbers of women with implants for a long enough period of time to evaluate whether or not implants cause cancer. A study by scientists from the NCI found that women with breast implants were more likely to die from brain cancer, lung cancer, other respiratory diseases, and suicide compared with other

plastic surgery patients.³⁰ The NCI study compared augmentation patients to other plastic surgery patients, who were very similar in socio-economic status, health status, and health habits (including smoking). Another strength of the study was that all the women had implants for at least seven years, which although not a long enough follow-up for a conclusive cancer study, is considerably longer than other implant studies.

A second NCI study found a 21% overall increased risk of cancer for women with implants, compared with women of the same age in the general population.³¹ The increase was primarily due to an increase in brain cancer, respiratory tract cancers, cervical cancer, and vulva cancer.

A Swedish study, Finnish study, and Danish study all found that women who have breast implants for augmentation were three times as likely to commit suicide as women in the general population of those countries.^{32, 33, 34} The Swedish and Danish studies also found a significant increased risk of lung cancer, but did not control for smoking. A recent study of mastectomy reconstruction patients in the U.S. also found a higher rate of suicide among implant patients compared to women who underwent mastectomies without reconstruction.³⁵

The statistically significant increase in suicide in five studies has been subject of considerable debate. Review articles funded by the American Society of Aesthetic Plastic Surgeons³⁶ and by Dow Corning³⁷ conclude that the increased risk of suicide is likely to predate implant surgery, and that women who choose breast implants are more likely to be depressed or have low self-esteem, as well as demographic traits that put them at higher risk of suicide. However, these assumptions are not supported by research data. One study pointed out that 8% of Danish augmentation patients had a psychiatric admission prior to augmentation surgery, compared to 6% of women undergoing other cosmetic procedures. However,

Danish women needed a psychiatric referral in order to qualify for free augmentation surgery, which could easily explain this small, non-significant difference.³⁸ Like other plastic surgery patients in an era where plastic surgery is quite common and generally accepted, patients tend to be less satisfied with the body part that they are having surgically altered, but not less satisfied with their general appearance or themselves.³⁹ Moreover, the most important demographic predictors of suicide, which are age, race, and sex, were already controlled in the studies finding an increased risk of suicide.

It is also important to note that a recent Danish study found an increase in depression among women who had undergone breast augmentation.¹² In that study, the women with breast implants were five to seven times more likely to be taking antidepressants than comparison samples of women who underwent breast reduction surgery or women of the same age from the general population. Among the augmentation patients, the women who had their implants removed and replaced at least once were more likely to be taking antidepressants than those who still had their original implants. Although it is impossible to determine whether the women were also more depressed prior to breast augmentation, the relationship between multiple surgeries and use of anti-depressants suggests that complications from the implants may contribute to depression.

General Health and Quality of Life

It is difficult to assess the impact of breast implants on health and mortality generally, because women who undergo breast augmentation tend to be healthier and more affluent than women in the general population. For example, NCI researchers found a lower mortality rate among augmentation patients compared to the general population of women their age, but a higher mortality rate among augmentation patients compared to other plastic surgery patients. The

authors concluded that plastic surgery patients are a more appropriate comparison sample, because they are similar in social class, health, health habits, and other key variables.³⁰

A Canadian study of women with implants compared to the general population of women of the same age found that augmentation patients were more than four times as likely to be hospitalized, experienced more hospitalizations, and visited physicians and specialists more often. In other words, augmentation patients cost the healthcare system significantly more than other patients of the same age and geographic location.⁴⁰

A recent study of women who had breast implants after mastectomy came to the surprising conclusion that women with implants had a significantly better survival rate than other women of similar age, race, and diagnosis.³⁵ However, a critique of that study by NCI researchers pointed out that the better survival rates could have been the result of other advantages of the implant sample: including less obesity, higher social class, better prognosis, treatment at designated cancer centers, and use of adjuvant treatment.⁴¹

It is often assumed that breast implants improve the self-esteem and quality of life of women who undergo augmentation, as well as those having reconstruction after breast cancer. However, the research does not support this assumption. Studies of augmentation patients show no difference or improvement in self-esteem, compared to women who do not undergo augmentation.³⁹ Studies by NCI researchers and other national experts indicate that women who have undergone reconstruction report the same quality of life as women who did not have reconstruction after mastectomy; in fact, implant patients are more likely to report that cancer harmed their sex life than women who underwent mastectomy without reconstruction.⁴² Self-selection makes it difficult to interpret these data, but the Inamed data

presented at the October 2003 FDA meeting indicated a decrease in all quality of life measures two years after implants compared to before surgery. Overall, these findings indicate that implants have yet to prove that they objectively improve women's quality of life.

The Hidden Costs

The initial surgery for breast implants is the first, but not the greatest expense for implant patients. If silicone breast implants last approximately 7-10 years before breaking, replacement surgery will add greatly to the cost. The implant itself may have a warrantee for free replacement, but the surgical and anesthesia costs are not free, nor are the costs of the medical facility. These expenses may not be affordable for all implant patients, especially since the initial breast augmentation is often available on an installment plan.

Cosmetic surgery is not covered by health insurance, and problems resulting from cosmetic surgery are usually excluded from coverage. In some states, major health insurance providers do not insure women with breast implants. Some insurers will sell health insurance to women with implants, but charge them more, and some insurers will not cover certain kinds of illnesses for women with breast implants, or not cover any problems in the breast area. For women who are diagnosed with diseases that are excluded, it will not matter if those diseases are unrelated to the implants.

What if a woman no longer wants breast implants? Implants can be removed and not replaced, but the breast tissue stretches from the implant, and the breast is unlikely to be as attractive as it was before the implant surgery.⁴³ Women with leaking silicone implants often lose breast tissue as part of the removal surgery. According to testimony presented at the October 2003 FDA meeting, this may result in surgery that is similar to a mastectomy.

Conclusions

In 1990, breast implants had been sold for more than 25 years but there were no published epidemiological studies or clinical trials. There are now dozens of studies of women with implants, most of them funded by Dow Corning or medical associations with a financial interest in the outcome. These studies are persuasive in showing that breast augmentation does not dramatically increase the risk of diseases in the short-term. A co-author of most of those studies, who served as a consultant to Inamed, argues that studies "with a mean follow-up of a decade and almost three decades of follow-up for the longest-term implant recipients" is "long enough."⁴⁴ However, the studies he cites and co-authored included many women with implants for only a few months or a few years, and therefore did not have the statistical power to draw meaningful conclusions about long-term safety. The small number of women providing relevant long-term data is especially a problem when studying diseases such as cancer, scleroderma, and lupus which take years to develop and diagnose. Careful scrutiny of the research indicates an increase in symptoms in many studies, but it is primarily in the studies where all the augmentation patients had implants for at least six years that increases in disease risks are statistically significant. It is also notable that the independently funded studies tend to focus on women with implants for longer periods of time, and often show increased risks that are not apparent in the industry-funded studies.

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