

## **Comment to the FDA Docket on the FDA's Draft Guidance to Improve Patient Communication on Breast Implants**

A Working Group comprised of two former presidents of the American Society of Plastic Surgeons, the president of a national research center, and four nationally respected patient advocates came together to find common ground regarding the risks of breast implants. As individuals (Dr. Scot Glasberg, Dr. Alan Matarasso, Dr. Diana Zuckerman, Ms. Karuna Jagger, Ms. Raylene Hollrah, Ms. Jamee Cook, and Ms. Maria Gmitro), we are urging that the FDA require a black box warning and Patient Informed Consent Check List that provides information about the risks of cancer, breast implant illness, and other serious health problems in explicit and easy-to-understand wording that all individuals considering breast implants can understand, regardless of educational level or stress that is inevitable when a person is considering surgery.

### **Black Box Warning**

The FDA's draft Black Box warning is too vaguely worded on BIA-ALCL and breast implant illness, and includes jargon that will not be understood by all patients. For example, it should specify that breast implants can **cause** ALCL, breast implants are **not** lifetime devices (instead of FDA's proposed Black Box wording that they are "not considered lifetime devices), replace technical jargon, and be more explicit about the evidence regarding breast implant illness instead of making it sound like it is not a real risk.

The FDA draft Black Box states that "breast implants have been associated with the development of a cancer of the immune system called breast implant-associated anaplastic large cell lymphoma (BIA-ALCL)." Association implies correlation rather than causation. In fact, the evidence is clear that breast implants can cause BIA-ALCL.

The FDA draft says that the rates of BIA-ALCL "are not well defined." Although correct, that terminology will not be understood by all patients. Instead, it should state that the rates "are not known."

We agree with the FDA draft that it is important to illustrate the seriousness of BIA-ALCL by stating that "Some patients have died from BIA-ALCL."

The draft Black Box wording regarding symptoms of breast implant illness would be confusing to patients. It refers to systemic symptoms, which is the correct term, but not one that all patients would understand. It does not mention breast implant illness, which although not an established medical term, is one that is well understood by patients. The FDA draft background paper and Black Box warning both state that "some" patients with breast implants "have reported a variety of systemic symptoms," which implies that the numbers of women with these symptoms is small and that they reported the symptoms but that they haven't been diagnosed. That is incorrect. The wording should be changed to "patients have experienced a variety of symptoms." The FDA proposed Black Box statement that "some

patients report complete resolution of symptoms” again implies that these improvements are reported but not medically confirmed.

On the contrary, a review of several well-designed studies by De Boer et al. (2017) found that most women with breast implant illness who had their implants removed and not replaced were confirmed by physicians to have complete or substantial improvement in their symptoms and overall health.

In addition, the FDA draft Black Box does not mention the risk of autoimmune/connective tissue diseases. The Black Box should specify that **“several studies suggest that women with silicone gel or saline-filled breast implants have a small but significant increase in their chances of developing certain autoimmune or connective tissue diseases.”** That statement is supported by the largest long-term study to date, by Watad et al. (2018), a retrospective analysis of 24,651 women with breast implants (confirmed by medical records) and 98,604 matched women who did not have breast implants. The strongest association with breast implants (OR>1.5, p<0.001) was recorded for Sjögren’s syndrome, systemic sclerosis (scleroderma) and sarcoidosis, based on new medical diagnoses made after the women received breast implants, which were included in medical records during a period of up to 20 years. In addition, (Coroneos et al. 2019) reported that Allergan’s study of 60% of the almost 50,000 women they enrolled in their study submitted to the FDA, physicians’ diagnoses of their patients two years after their implant surgery found statistically significant increases in fibromyalgia, rheumatoid arthritis, and lupus compared to the general population. Although the Mentor data reported in that study are very flawed, the Allergan data, which were provided to the FDA, seem solid.

## **Patient Informed Consent Checklist**

The Breast Implant Working Group created a checklist that was provided to the FDA in October. This checklist has been endorsed by the **American Society of Plastic Surgeons, the National Center for Health Research, Breast Cancer Action, Our Bodies Ourselves, National Women’s Health Network, Jacobs Institute for Women’s Health, Breast Implant Victims Advocacy, Just Call Me Ray, and Breast Implant Safety Alliance.** It was also supported by more than 77,000 individuals who signed a petition that the Working Group provided to FDA officials on December 9, 2019

We agree with the FDA that the purpose of a patient checklist is to provide information for patients considering breast implants for augmentation or reconstruction, so that they can carefully weigh the risks and benefits of breast implants and make the decision that is right for them. Based on our experience with patients, we urge the FDA to ensure that the checklist is:

- **Brief and easy-to-understand, formatted with information on specific issues that are presented succinctly;**
- **Jargon-free.** Keep in mind that the average reading level in the U.S. is 6<sup>th</sup> grade.
- **Organized to focus on the information that patients are less likely to obtain from other sources. It should not start with lengthy sections that are not especially interesting to patients.**

## Focus and Organization of the Checklist

**The goal of the checklist should be to provide the most essential information that patients might not get from standard informed consent forms. It is therefore essential that the checklist provide information that thousands of implant patients have stated they were not warned about.** For that reason, the checklist **should not focus on surgical and cosmetic risks**, which are the types of risks that all patients are warned about in standard consent forms. Instead of the almost full page of mostly surgical risks that are listed at the beginning of the FDA’s draft checklist, such risks should be summarized very briefly in one sentence, with the checklist focused on other risks that patients could otherwise not be aware of. **Similarly, cosmetic and local risks should be listed last in the checklist**, since that information is more likely to be provided through other means.

The FDA draft checklist starts with “Considerations for a Candidate for Successful Breast Implantation,” cancer risk and a short section on “systemic illness.” We suggest shorter, more focused headings and information to make the checklist more engaging and easy to read.

### **Who shouldn’t get breast implants?**

The above heading should replace “Considerations for a Candidate for Successful Breast Implantation,” since that latter heading implies that the patient characteristics listed are the only ones that would reduce the chances of complications or other problems. **In terms of content, the FDA draft wording on who should not get breast implants contains important information but is much too long and includes information that could be summarized.** The goal of the checklist should be to provide the most essential information that patients might not get from standard informed consent forms. We recommend a short summary regarding active infections, cancer, or wound healing, and the following wording instead:

*I understand that the safety of breast implants was never studied for people who have autoimmune symptoms or diseases, or a family history of those diseases. Breast implants may be more likely to cause serious health problems and symptoms for these people. In addition, breast implants may not be safe for anyone with a weakened immune system or certain genetic risk factors that have not yet been identified.*

### **Risk of Cancer: BIA-ALCL (Breast Implant Associated Anaplastic Large Cell Lymphoma)**

We recommend that the FDA’s draft wording for BIA-ALCL could be improved as follows:

*I understand that there is a small risk for me to develop BIA-ALCL, a cancer of the immune system. BIA-ALCL is a type of lymphoma that develops on or around the scar capsule that surrounds the breast implant. I understand that the symptoms of BIA-ALCL include breast swelling, lumps, pain, and asymmetry that develop after surgical incisions are completely healed, usually years after implant surgery.*

*Treatment for BIA-ALCL includes removal of the implant and scar capsule, and, if not treated early, may include chemotherapy and radiation. This diagnosis and treatment may be at my own expense and is not always covered by insurance.*

## **Systemic Symptoms: Breast Implant Illness**

**As noted earlier, “Breast Implant Illness” should be the term used, since “systemic symptoms” is not a term that all patients would understand.** Also as noted earlier, the FDA draft guidance and draft checklist consistently imply that the number of women reporting symptoms of breast implant illness is small and that there is no research evidence that the symptoms are caused by their implants. For example, the FDA’s draft wording that “some women report” implies that a small number of women are claiming an illness that isn’t real. It is more accurate and meaningful to patients to say that **several studies support the apparent causal link to breast implant illness symptoms** (Watad et al 2017 and Colaris et al. 2017) **and to symptom improvement after implants are removed** (DeBoer et al. 2017), for example). It should also state that the largest, long-term studies also indicate a statistically significant increase in certain autoimmune or connective tissue diseases, as summarized on page 2 of this document, citing Watad et al. 2018 and Coroneos et al. 2019). For that reason, ASPS, researchers, women’s health organizations, and patient groups endorse the following wording:

*I understand that because of the lack of long-term safety data, we are still learning about the health problems that result from breast implants. To date, thousands of women have reported to the FDA or to researchers that they have experienced serious health problems that several studies have linked to their breast implants. This may occur either immediately after getting implants or years later. These often include symptoms such as: joint and muscle pain or weakness, memory and concentration problems, chronic pain, depression, fatigue, chronic flu-like symptoms, migraines, or rashes and skin problems.*

*Several studies of women with breast implants have shown that they are significantly more likely to be diagnosed with one or more of the following diseases compared to other women: Chronic Fatigue Syndrome; Multiple Sclerosis (MS); Rheumatoid Arthritis (RA); Sjögren’s syndrome; and Systemic Sclerosis/Scleroderma.*

*Although women who develop these symptoms or diseases can’t be certain that they were caused by breast implants, several studies indicate that most symptoms improve partially or completely after having their implants and capsules removed.*

## **Breast-Implant Specific Risks**

This heading in the FDA’s draft Checklist is misleading, since BIA-ALCL and many other risks of breast implants are specific to breast implants. More important, this section is much too long and includes too many topic areas.

We therefore recommend the following shorter, more specific sections:

## **How long do breast implants last?**

It's essential that patients understand what it means when experts say that breast implants "don't last a lifetime." Since many implant patients are young, some think that means they only last 30-50 years. Even saying "the longer you have them, the more likely they are to break" can be misinterpreted to refer to 30 or 40 years later. For that reason, the Working Group Checklist specifies "Implants may rupture or leak at any time, and that is more likely the longer you have them" and that "it is likely that I will need other surgeries related to my breast implants over the course of my life."

The wording should be succinct, explicit, and easy to understand. Augmentation patients are already aware that their insurance policy does not cover cosmetic surgery, but it is important for them to also know that insurance is unlikely to cover subsequent surgeries due to complications or breakage, since they might mistakenly assume that problems related to implants will be covered even if the initial cosmetic surgery is not. We recommend the following wording:

*I understand that breast implants are not expected to last for the rest of my life. Implants may rupture or leak at any time, and that is more likely the longer you have them. In addition, it is likely that I will need other surgeries related to my breast implants over the course of my life. If I am a cosmetic surgery patient, my health insurance policy may refuse to cover these surgeries for removal, and probably would not cover replacement. These additional surgeries and procedures can include implant removal with or without replacement, muscle and tissue repair, scar revisions, MRI diagnostic exams, or other procedures. I understand that undergoing multiple surgeries may increase my chances of permanent breast deformity.*

## **Chemicals and Metals in Breast Implants**

Patients should be informed about the chemicals and metals in the specific make and model of breast implants they are considering. Since the checklist is for all breast implant patients, it should include a brief, general statement about chemicals and heavy metals, but each patient should get separate, more detailed information about the specific model of implant they are considering. We recommend the following wording for the checklist:

*I understand that all breast implants contain chemicals and small amounts of heavy metals that may cause health problems. I understand that most of these chemicals are confined to the shell of the implant or stay inside the shell. However, small quantities have been found to diffuse (bleed) from or through the implant shell, even if the implant is intact and not ruptured.*

## **Rupture and Leakage**

Patients would benefit from a section with a heading of "Rupture and Leakage." Although this overlaps with the issue of how long implants last, more specific information about silent rupture is important.

We recommend the following wording for the checklist, understanding that if FDA no longer recommends MRIs after 3 years, that wording should be revised, but the explicit information about the risks of silicone migration should be included:

*I understand that the longer my breast implants are in place, the more likely they are to rupture, especially after the first few years. When a saline implant ruptures, it usually deflates quickly. When a silicone gel implant ruptures, I may not notice any changes and the rupture may not be detected by my doctor or by mammogram, MRI, or sonogram. I understand that an MRI is recommended for silicone gel breast implants 3 years following surgery and every 2 years after that to check for silent rupture, and that these MRIs often are not covered by health insurance. I understand that silicone may migrate from the implant into nearby tissues such as the chest wall, lymph nodes, upper abdominal wall, and into organs such as the liver or lungs where it cannot be removed. Since migrated silicone can cause health problems, it is currently recommended that any ruptured silicone implant should be removed as soon as possible. I understand that, if needed, treatment of these conditions may be at my own expense and not covered by insurance or a manufacturer warranty.*

## **Capsular Contracture**

Capsular Contracture is a common complication that therefore should have its own heading. Our recommended wording is as follows:

*I understand that one of the most common complications of breast implants is when the scar tissue capsule that forms around the implant hardens. In some cases, this can be quite painful, distort the shape of the breast, and can make mammography more painful and less accurate. Removing the implant and capsule without replacing the implant is the only recommended way to guarantee that this problem is corrected.*

## **Breast Cancer**

Breast cancer issues should be a separate heading in the checklist, not part of the section on ACLC, in order to avoid confusion. Our recommended wording is as follows:

*I understand that all breast implants can interfere with mammography and breast exams, possibly delaying the diagnosis of breast cancer. I understand that if I get breast implants, I should inform the mammography technologist about the implants and ask for additional views to improve the accuracy. I understand that mammography can also cause the breast implant to rupture or leak.*

## Interference with Breastfeeding

Since the data are lacking, our recommended wording is as follows:

*I understand that breast implants and breast surgery may interfere with my ability to successfully breastfeed. No long-term research has been conducted to determine the possible transmission of chemicals and heavy metals in the breast milk of women with implants.*

## Loss of Sensation to Breast or Nipple(s)

Many women do not understand that breast implant surgery can cause loss of sensation. While more likely among reconstruction patients, it is important to note that augmentation patients can also experience loss of sensation or painful sensitivity. We therefore recommend this wording:

*I understand that breast implants and breast surgery may cause the nipple or breast to be painful, or to have decreased sensation. These changes may be temporary or permanent, and may affect sexual response or the ability to nurse a baby.*

## Cosmetic Complications

Cosmetic complications should be the last section of the checklist, because like surgical complications they are often included in standard informed consent documents. We recommend the following brief, easy to understand, but explicit warnings, such as using the term “sag” instead of ptosis:

*I understand that if my breasts had slightly different shapes before surgery, they may remain slightly different after surgery. I understand that the implants may cause the breasts to look slightly different in size or shape. I understand that the implant may move from the original placement location and that may result in asymmetry or other cosmetic problems. Breast implants can cause the breasts to sag over time due to the weight of the implants. I understand that if I am not happy with the results, I may need future surgeries to improve the appearance of my breasts.*

## FOOTNOTES:

Colaris MJ, de Boer M, van der Hulst RR, Cohen Tervaert JW. (2017) Two hundred cases of ASIA syndrome following silicone implants: a comparative study of 30 years and a review of current literature. *Immunologic Research* 65(1):120-128. doi: 10.1007/s12026-016-8821-y.

Coroneos C, Selber J, Offodile A, et al. (2019) US FDA breast implant postapproval studies: Long-term outcomes in 99,993 patients. *Annals of Surgery* 269(1):30-36. doi: 10.1097/SLA.0000000000002990

De Boer M, Colaris M, van der Hulst RR, Cohen Tervaert JW (2017) Is explantation of silicone breast implants useful in patients with complaints? *Immunologic Research* 65(1):25-36. doi: 10.1007/s12026-016-8813-y.

Watad A, Quaresma M, Brown S, et al (2017) Autoimmune/inflammatory syndrome induced by adjuvants (Shoenfeld's syndrome)—an update. *Lupus* 26(7):675-681 doi:10.1177/0961203316686406

Watad A, Rosenberg V, Tiasano S. et al. (2018) Silicone breast implants and the risk of autoimmune/rheumatic disorders: A real-world analysis. *International Journal of Epidemiology*. 47(6):1846-1854. doi: 10.1093/ije/dyy217.