How two manufacturers demonstrate the safety profile of breast implants

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Hearing on the SCHEER preliminary Opinion on the safety of breast implants
in relation to anaplastic large cell lymphoma (BIA-ALCL)

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Breast implants designed for intended purpose

State of the art standards mandatory for design

EN ISO 14607 – European and Global standard for mammary implants

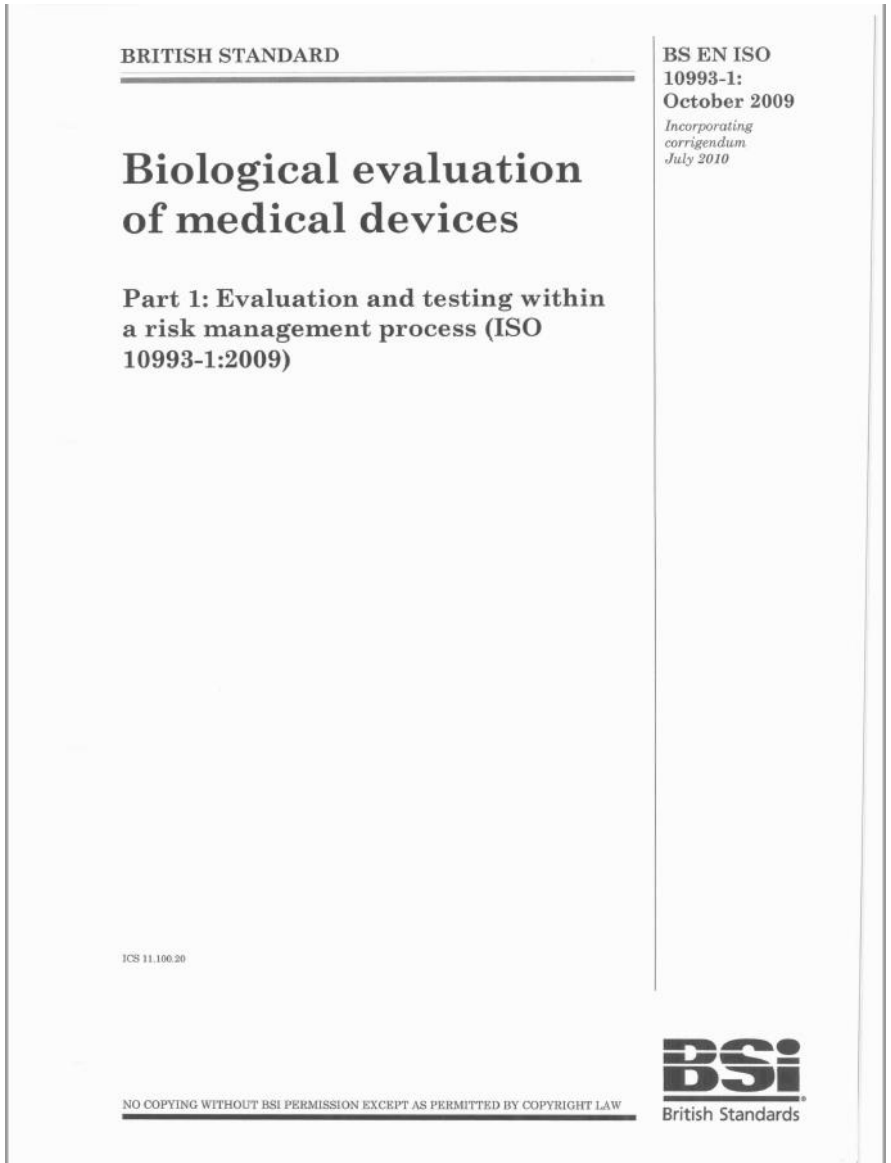
Scope – with regards to safety…specifies requirements for intended performance, design attributes, materials , design evaluation, manufacturing, packaging, sterilisation, and information supplied by the manufacturer

Safety is assured through:

- **Materials compatibility**
  - Characterisation
  - Cytotoxicity
  - Trace elements
  - Low molecular weight oligomers

- **Design Evaluation**
  - Chemical evaluation
  - Mechanical tests
  - Physical evaluation
  - Biological evaluation

State of the art standards mandatory for design



BRITISH STANDARD

BS EN ISO 10993-1: October 2009

Incorporating corrigendum July 2010

Biological evaluation of medical devices

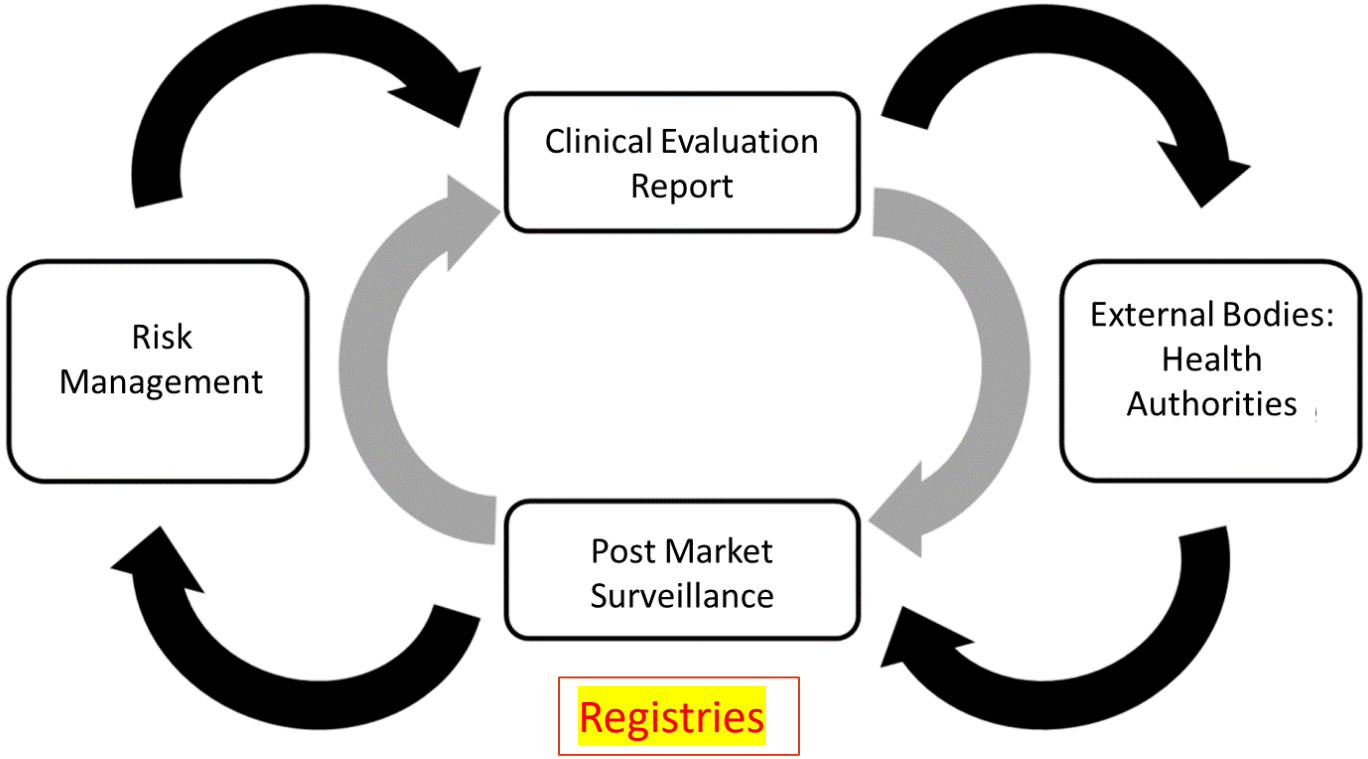
Part 1: Evaluation and testing within a risk management process (ISO 10993-1:2009)

ICS 11.100.20

BSI British Standards

- >20 standards define Breast implants testing
- All breast implants evaluated/tested for biological safety for permanent implantation
- Animal and in vitro models used
- Risk Management process
- Multiple safety endpoints demonstrated:
  - Non-Carcinogenic
  - Non Genotoxic
  - Non-Cytotoxic
  - Non-Sensitising
  - Non-Irritating
  - Not Systemic toxicity
  - Implantation safety
  - No chronic toxicity

Clinical Risk Management



Numerator/denominator /Implants history

- Clinical Evaluation Report is a living document → updated yearly
- Report contains analysis of:
  - Published clinical data
  - Ongoing clinical trials/ data
  - Post Market Surveillance
- No CER = No CE mark for selling in the European Markets
- Assessed by external notified bodies to assure that all patient risks have been considered
- Proves that the device in question achieves its intended purpose safely

Patient leaflet provides risk benefit for informed decision

Patient information regarding BIA-ALCL

" European safety information, the US FDA and current scientific literature have identified an association between breast implants and the development of cancer called breast implant associated anaplastic large cell lymphoma (BIA-ALCL). This cancer occurs more commonly in patients with textured breast implants rather than smooth implants and typically develops many years after surgery. At this time rates of BIA-ALCL are considered to be low. In most patients BIA-ALCL is found within the fluid or scar tissue next to the implant in rare cases persistent swelling or pain within the breast area can be signs of BIA-ALCL. It is important to obtain medical advice if you suffer from either of these symptoms. You physician will collect fresh fluid from the breast area for testing and if positive the most common treatment is removal of the implant and scar tissue surrounding the area; however some patients may require treatment with chemotherapy/radiation therapy. Although treatment is usually successful some patients have died from BIA-ALCL hence, early treatment is essential"

-GC Aesthetics Patient Leaflet 2020

Published clinical data demonstrates need for textured breast implants

Clinical Benefits of Textured over Smooth breast implants

- Capsular contracture is one of the most significant complication associated with breast implants [1, 2]
- Continues to be the leading cause of morbidity and reoperation following breast surgery, with reported incidences as high as 19%[3]
- Recent meta-analysis of 4,486 patients, with 8,867 implants showed that the smooth implants were more likely to be associated with capsular contracture with a relative risk of 3.76 (95% CI 2.65–5.32) compared to textured implants [4]
- Banning textured implants produces 1 additional death by 50 patients and approximately 3000 reoperations [5]
- Other complications, such as malposition and secondary procedures have been documented in the literature and the data shows that their incidence is reduced with textured versus smooth devices[6]
- Risk of rotation is reduced with use of anatomically shaped textured implants[7]

Textured implants are needed to prevent sub-optimal patient outcomes in certain conditions and exposure to risks associated with re-operations and increased morbidities.

1. Headon H, Kasem A, Mokbel K. Capsular Contracture after Breast Augmentation: An Update for Clinical Practice. Arch Plast Surg. 2015 Sep;42(5):532-43. doi: 10.5999/aps.2015.42.5.532. Epub 2015 Sep 15. PMID: 26430623; PMCID: PMC4579163
2. Adams WP Jr. Capsular contracture: what is it? What causes it? How can it be prevented and managed? Clin Plast Surg. 2009 Jan;36(1):119-26, vii. doi: 10.1016/j.cps.2008.08.007. PMID: 19055967
3. Calobrace MB, Stevens WG, Capizzi PJ, Cohen R, Godinez T, Beckstrand M. Risk Factor Analysis for Capsular Contracture: A 10-Year Sientra Study Using Round, Smooth, and Textured Implants for Breast Augmentation. Plast Reconstr Surg. 2018 Apr;141(4S Sientra Shaped and Round Cohesive Gel Implants):20S-28S. doi: 10.1097/PRS.0000000000004351. PMID: 29595715.
4. Liu X, Zhou L, Pan F, Gao Y, Yuan X, Fan D. Comparison of the postoperative incidence rate of capsular contracture among different breast implants: a cumulative meta-analysis. PLoS One. 2015 Feb 13;10(2):e0116071. doi: 10.1371/journal.pone.0116071. PMID: 25680100; PMCID: PMC4332657.
5. Danilla SV, Jara RP, Miranda F, Bencina F, Aguirre M, Troncoso E, Erazo CA, Andrades PR, Sepulveda SL, Albornoz CR. Is Banning Texturized Implants to Prevent Breast Implant-Associated Anaplastic Large Cell Lymphoma a Rational Decision? A Meta-Analysis and Cost-Effectiveness Study. Aesthet Surg J. 2020 Jun 15;40(7):721-731. doi: 10.1093/asj/sjz343. PMID: 31761953
6. Namnoum JD, Largent J, Kaplan HM, Oefelein MG, Brown MH. Primary breast augmentation clinical trial outcomes stratified by surgical incision, anatomical placement and implant device type. J Plast Reconstr Aesthet Surg. 2013 Sep;66(9):1165-72. doi: 10.1016/j.bjps.2013.04.046. Epub 2013 May 9. PMID: 23664574.
7. Atlan, M., Bigerelle, M., Larreta-garde, V. et al. Characterization of Breast Implant Surfaces, Shapes, and Biomechanics: A Comparison of High Cohesive Anatomically Shaped Textured Silicone, Breast Implants from Three Different Manufacturers. Aesth Plast Surg 40, 89–97 (2016). https://doi.org/10.1007/s00266-015-0603-8

Breast implant surfaces - not all texture is the same

- Current classifications systems do not provide consistent data on product classification between manufacturers:
  - De Boer et al (2018)
  - Atlan et al (2018)
  - Jones et al (2018)
  - Barr et al (2017)
  - ISO 14607 (2018)

- ISO 14607 (2018) is the most widely accepted standard but has limitations:
  - Macro texture originates from marketing not science
  - Classification is based on **broad arbitrary categories** of surface roughness not linked to safety characterisation
  - **Smooth** (<10micron), **Micro** (10-50 Micron) or **Macro** (>50 Micron) surface roughness
  - Not all 'macro' or 'micro' textured surfaces are the same
    - Texturing of breast implants can be achieved in a number of **different ways**
    - Manufacturing technologies have evolved separately even for salt loss - different manufacturing environment, equipment, processes, silicone part numbers, texturing materials
    - Other characteristics are also required to characterise the surface - including Pore size & diameter, kurtosis, skewness

- Scientific data does NOT support 'bundling' surfaces together into same risk category

- Safety assessment should be based on individual safety profiles of implants not classification systems

Clinical Benefits of ‘Macrotextured’ vs. ‘Microtextured’ breast implants

There is an array of clinical evidence available demonstrating the benefits of macro textured devices in comparison to micro textured breast implants.

Macro textured breast implants have been reported to offer lower rates of:

- **Capsular contracture**[1, 3, 5]
- **Malposition**[1]
- **Rippling**[1, 3]
- **Rotation**[1]

While demonstrating a better stability due to tissue adherence.

1. Maxwell *et al.* Benefits and Limitations of Macrotextured Breast Implants and Consensus Recommendations for Optimizing Their Effectiveness. *Aesth Surg J*. 2014; 34; 876 – 881.
2. Jewell and Jewell. A Comparison of Outcomes Involving Highly Cohesive, Form-Stable Breast Implants From Two Manufacturers in Patients Undergoing Primary Breast Augmentation. *Aesth Surg J.* 2010; 30; 51 – 65.
3. Abramo *et al*. How Texture-Inducing Contraction Vectors Affect the Fibrous Capsule Shrinkage Around Breast Implants? *Aesth Plast Surg*. 2010; 34; 555-560.
4. Danino *et al.* Comparison of the Capsular Response to the Biocell RTV and Mentor 1600 Siltex Breast Implant Surface Texturing: A Scanning Electron Microscopic Study. *Plast Reconstr Surg.* 2001; 108; 2047 – 2052. 1.
5. Hedén, P., Montemurro, P., Adams, W P. Jr., Germann, G., Scheflan, M., Maxwell, G. P. *Anatomical and Round Breast Implants: How to Select and Indications for Use*. Plastic and Reconstructive Surgery. 2015; 136; 263–272

Alternative procedures for breast augmentation

Alternative Option	Description	Advantage	Disadvantages	Limitations
Silicone Injections	Silicone injected in to the breast.	Cheaper	Illegal as substances used are unregulated. Substances can travel to different parts of the body through the bloodstream. High rate of complications and risk of death. High risk of cysts and skin necrosis.	Not intended for use in this manner.
Autologous Fat Transfer **Fat Grafting** **Fat Injections**	Fat is taken from other parts of the body and transferred or injected to the breast.	Natural feel Less risk of complications or allergic reactions *as no foreign body present.* Achieves good aesthetic results	Only an option for patients with spare body fat. Reabsorption of the fat can occur. This can also cause asymmetry. Furthermore, fat transfer requires several procedures to achieve the desired aesthetic outcome.	May not achieve long-term results due to reabsorption.

The use of breast implants is state of the art treatment for breast augmentation

BIA-ALCL Global Scope

Global cases as reported to the FDA- January 2020

84% of global cases were associated with Allergan breast implants [1]

*1% of cases were from other manufacturer including Bristol Myers, Squib, **Nagor**, Polytech Silimed, Silimed and Sientra/Silimed* [1]

- The US FDA reported **620** of the **733** globally BIA ALCL cases were associated with **Allergan breast implants**.
- The second manufacturer with more cases is **Mentor** (50 cases of 733).

[1] FDA. Medical Device Reports of Breast Implant-Associated Anaplastic Large Cell Lymphoma. Content current as of August 2020

Conclusions –

- Products are designed for their intended purpose to assure safety – remains a rare condition
- Risk mitigation and risk/benefit evaluation is carried out continuously for each product through clinical evaluation and post market surveillance
- Clear patient information continues to be needed for every product with the risks and possible complications to ensure the patient has all the facts to make balanced decisions.
- Textured implants are needed to prevent sub-optimal patient outcomes in certain conditions and exposure to risks associated with re-operations and increased morbidities.
- Not all texture is the same – **better individual technical/safety characterisation related to clinical performance**
- **Need standardised methology for calculating and communicating BIA-ALCL rates –** numerator/denominator **(ISO)**
- Better surveillance of BIA-ALCL cases numerator and denominator needed – **benefits of registries for systematic determination of risk – evolution of data collection data .**

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Thank you!