

# Scientific Committee on Health Environmental and Emerging Risks

## (SCHEER)

### Request for a scientific opinion on the safety of breast implants

#### in relation to anaplastic large cell lymphoma

#### 1. Background

Breast implant associated anaplastic large cell lymphoma (BIA-ALCL) is a rare sub type of non-Hodgkin's lymphoma. In 2016, World Health Organisation (WHO) defined specific diagnostic criteria for this rare disease.

BIA-ALCL is not a cancer of the breast tissue and the prognostic of the disease is generally favourable. The exact number of cases remains difficult to determine due to significant limitations in worldwide reporting. In addition, due to lack of global breast implant sales data, it is difficult to put this number into context. It has been estimated that 5 to 10 million women have received breast implants worldwide, with some estimations going as high as 35<sup>1</sup> million.

The U.S. Food and Drug Administration received in total 660 BIA-ALCL related medical devices reports (MDRs) until September 2018. After eliminating the duplicates a total of 457 unique MDRs for BIA-ALCL were identified. It is acknowledged by FDA that although the MDR system is a valuable source of information it may contain incomplete, inaccurate, untimely, unverified, or biased data<sup>2</sup>.

In January 2019, the Australian Therapeutic Goods Administration reported 78 confirmed cases of anaplastic large cell lymphoma in Australian patients<sup>3</sup>.

In April 2019, Health Canada reported 28 confirmed Canadian cases of BIA-ALCL<sup>4</sup>.

At EU level by March 2019, 243 cases were reported to the EU competent Authorities, out of which 211 were confirmed cases of BIA-ALCL. Of the confirmed cases, 166 were reported to be linked to textured implants at the time of diagnosis. The surface texture of the implants in the other reports remains unknown.

A number of competing theories are available to explain the causation of BIA-ALCL, such as bacterial contamination & biofilm formation leading to inflammatory and immune response; surface of the shell leading to chronic low-level inflammatory reaction; the shell shedding micro-particles that trigger an immune response; specific genetic reaction to implants; compounded chronic inflammatory reaction. As the pathogenesis of the disease has not yet been established and may be either on the implant side, e.g. low level of chronic inflammation induced by the shell, or on the surgical intervention side, e.g. bacterial contamination, or on the characteristics of the implant recipient, e.g. genetic characteristics of the patient, the best ways to address the matter is not yet identified.

Internationally, there have been some reports of BIA-ALCL associated with smooth breast implants at the time of diagnosis, however, the previous implant histories for these reports are unknown<sup>5</sup>. The predominance of the reports of BIA-ALCL have been reported in patients with textured implants at the time of diagnosis.

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<sup>1</sup> <https://www.ncbi.nlm.nih.gov/pubmed/29036945>

<sup>2</sup> <https://www.fda.gov/medicaldevices/productsandmedicalprocedures/implantsandprosthetics/breastimplants/ucm239995.htm>

<sup>3</sup> <https://www.tga.gov.au/alert/breast-implants-and-anaplastic-large-cell-lymphoma>

<sup>4</sup> <http://healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2019/69052a-eng.php>

<sup>5</sup> <https://www.fda.gov/medical-devices/breast-implants/breast-implant-associated-anaplastic-large-cell-lymphoma-bia-alcl>

When addressing questions about the continued availability of textured implants, an important consideration is that surface textures of breast implants are not all manufactured in the same way. Some literature studies report that they appear to be associated with different levels of risk. Anatomically shaped implants are commonly textured in some way. Clinically, the choice between round and anatomically shaped implants is determined by anatomic aspects of the chest wall, and the patient's preferred aesthetic outcome.

The use of textured implants is preferred in most European countries to prevent the undesirable movement or rotation of the implants, and are considered by some clinicians to reduce the risk of capsular contracture, which is often cited as the most common cause of revision in smooth implants. Movement or rotation is particularly undesired with anatomical implants, as this could result in an unacceptable aesthetic outcome. Additionally, there are a limited number of alternatives to the use of textured implants, and the alternatives are also associated with their own risks and contraindications.

Currently there is no international consensus on a single classification system for surface texture. A harmonised classification system would need to be established in order to collate scientific evidence on the risks and benefits of each type.

The Scientific Committee on Health, Environmental and Emerging Risks (SCHEER) advised in October 2017<sup>6</sup>, that there was insufficient scientific information available to establish a methodologically robust risk assessment to investigate a possible association of breast implants with ALCL development. However, it was recommended that a more in-depth evaluation be conducted on the possible association of breast implants with the development of ALCL. A significant body of scientific information was published in the meantime.

The rate of diagnosis of BIA-ALCL has rising over the past years. The information to date suggests that women with breast implants may have a very low but increased risk of developing ALCL while the rarity of the disease makes it difficult to establish a definite causal relationship. Given the increase in confirmed and unconfirmed reports of BIA-ALCL, we may be confronted with an emerging health risk and SCHEER should provide an opinion on the safety of breast implants in relation to anaplastic large cell lymphoma.

When providing the opinion, given the rarity of the disease, the participation of experts and stakeholders at a global level is deemed necessary. This includes contacts with breast implant registries at national and international level whenever possible. For the global context, the Committee will make use of the SCHEER Rules of Procedure.

## **2. Terms of reference**

In the light of the above considerations, the Scientific Committee on Health Environmental and Emerging Risks (SCHEER) is requested to provide a scientific opinion on 'The safety of breast implants in relation to anaplastic large cell lymphoma'.

In particular, the SCHEER is asked:

1. To briefly describe what are the specific clinical indications and uses for various types of breast implants.
2. To briefly describe what BIA-ALCL is, what the specific diagnostic criteria are, what the state of the art treatment is, and what the prognosis of the disease is. In relation to ALCL the state of the art of good clinical practices for the follow-up of women with breast implants should also be described.

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<sup>6</sup> [https://ec.europa.eu/health/sites/health/files/scientific\\_committees/scheer/docs/scheer\\_o\\_007.pdf](https://ec.europa.eu/health/sites/health/files/scientific_committees/scheer/docs/scheer_o_007.pdf)

3. To indicate what is the state of the art knowledge in terms of incidence of BIA-ALCL.
4. To describe the state of the art knowledge regarding the characterisation and classification of textures of the breast implant shells (e.g. is classification possible?).
5. To indicate whether a causal relationship between breast implants and ALCL can be established based on the evidence available to date. To discuss what may be the potential and if possible the most plausible pathogenesis mechanisms. To evaluate the available information on incubation time, and in relation to this, discuss the importance of knowledge on previous implants history of women developing BIA-ALCL. To evaluate if preventive explantation is warranted in case reasons for concern related to breast implants or specific subcategories of breast implants are identified.
6. To describe the factors that may determine the risk of BIA-ALCL. To identify criteria regarding the characterisation of breast implants in relation to ALCL and control measures to reduce the identified risk.
7. In the context of ALCL to briefly describe alternatives to breast implants.
8. Where relevant to identify needs for further research and the best ways to collect the missing data regarding breast implants and ALCL.

The considerations should cover both reconstructive and augmentation use of breast implants.

### **3. Deadline**

31 August 2020