


Comments received during the public consultation on the SCHEER preliminary opinion on "*The safety of breast implants in relation to anaplastic large cell lymphoma (BIA-ALCL)*"

	Name of individual/organisation	Table of contents	DJ	attach	SCHEER's response
1	Geertsma Robert, RIVM - National Institute for Public Health and the Environment, Netherlands	ABSTRACT	<p>Abstract, lines 23-24</p> <p>The statement "Overall there is a moderate level of evidence for a causal relationship between textured breast implants and ALCL" implies that a causal relationship exists between ALCL and all types of textured implants. As can be concluded from multiple statements in the body of the Opinion, stratification between the relative risks of various types of textures (including no texture) is currently not possible. In order to provide an honest and complete picture of current knowledge, this should be explained carefully in the Opinion, and certainly also in the Abstract, which is likely to undergo a much broader dissemination than the entire report. Furthermore, it is important also to point out that implants with different surface textures may also have different benefits, so in order to draw conclusions, a full benefit-risk evaluation should be made.</p> <p>In relation to this, SCHEER should consider including a statement in the abstract on the need for an unambiguous, uniform classification of different surface textures with more parameters than just "surface roughness".</p>		<p>SCHEER agrees with this comment and has adapted the text of the Opinion for further clarification.</p> <p>Modified text:</p> <p>"Overall SCHEER considers that there is a moderate weight of evidence for a causal relationship between textured breast implants and BIA-ALCL, particularly in relation to implants with an intermediate to high surface roughness.</p> <p>At this point it should be noted that i) there are several types of textured implants ii) surface textures of breast implants are not all manufactured in the same way, and iii) implants with diverse surface textures may also present different benefits. The magnitude of the risk per type of textured implant is difficult to establish due to the low incidence of the risk. Even with macro-textured implants, BIA-ALCL has a very low incidence. Therefore, risk assessments per implant type are needed. Furthermore, the risk should be weighed against the benefits. There is also a need for an unambiguous, clinically validated classification system for breast implants including more parameters than just "surface roughness". A history of textured breast implants/expanders appears to be necessary but not sufficient for the development of BIA-ALCL."</p>
2	No agreement to disclose personal data	ABSTRACT	<p>General comment Could the SCHEER further describe possible risk mitigation of using micro-textured implants rather than macro-textured implants?</p>		<p>At the moment, this is not possible in view of the lack of information concerning types of implant used in individual patients. However, it may be possible to obtain this information in the future based on data being accrued by ongoing breast implant registrations.</p>

3	No agreement to disclose personal data	ABSTRACT	<p>Page 2, line 4-5 General comment – in the first line of the abstract ‘The SCHEER was requested ... to provide a scientific opinion on the safety of breast implants ...’ regarding ALCL.</p> <p>Page 35, line 22-23 notes ‘Breast implants carry a reasonable assurance of safety and efficacy in that they perform as they were intended.’ Why have the SCHEER group applied the US FDA clinical evidence standard for market access (reasonable assurance safety/efficacy) rather than the one (safety and performance as intended by the manufacturer)? Has the SCHEER engaged with notified bodies to support this conclusion? Have the SCHEER considered the regulatory status of these products in jurisdictions that apply an efficacy standard for market access to support this conclusion?</p>	<p>SCHEER as an independent advisory committee has not engaged specifically with Notified Bodies on this subject. However, Notified Bodies were invited to the hearing that took place on November 16<sup>th</sup> 2020. SCHEER did not choose any specific wording for the safety and performance issues of breast implants. The basis for this was the new MDR. All medical devices carry an inherent risk when applied to patients. The regulatory status that was followed by SCHEER was the new MDR that should have been implemented in May 2020. In view of the Corona pandemic this has been postponed to May 2021. In the MDR, the benefit of using a medical device including breast implants, needs to be weighed against the risk for the patient. This benefit-risk analysis needs to be documented.</p> <p>Page35 line 22-23. Reference added.</p> <p>“Breast implants carry a reasonable assurance of safety and efficacy in that they perform as they were intended as indicated by the long term follow-up evaluated by Calobrace et al. (Calobrace et al. 2018).</p>
e4	Zambon marzia, Europa Donna The European Breast Cancer Coalition(submission on behalf of the Board of Directors), Italy	ABSTRACT	<p>Breast implants safety and Anaplastic Large Cell Lymphoma &gt; SCHEER Preliminary Opinion - Answer to Consultation by Europa Donna – The European Breast Cancer Coalition's Board of Directors As requested by the European Commission, the Scientific Committee on Health, Environmental and Emerging Risks (SCHEER) provided an opinion on the safety of breast implants in relation to anaplastic large cell lymphoma (BIA-ALCL). The main purpose of the scientific opinion was to assist the Commission in assessing the most recent scientific and technical information on breast implants in relation to anaplastic large cell lymphoma (BIA-ALCL).</p> <p>As the European Breast Cancer Coalition and patient advocates, we are very concerned with the problem of safety of breast implants and we are well aware of the positions being taken by medical regulatory authorities in Europe and elsewhere in the world, including the SCHEER preliminary opinion and its possible consequences, so we are closely</p>	<p>SCHEER agrees with this comment in that the choice of breast implant should not be driven by commercial aspects, but rather by the most appropriate implant for that specific patient with selection based on the most up-to-date scientific evidence available. Indeed, patients should be given the opportunity to explore all appropriate alternative options for surgical breast reconstruction. A shared consultation with a multidisciplinary healthcare team including a pathologist, oncologist, surgeon, breast care nurse, etc., should be held with the patient to allow informed decision making to take place with regards to the breast reconstruction procedure as well as the choice of implant. Indeed, all aspects of breast reconstruction should be evaluated and discussed with the patient, expressly covering advantages, disadvantages, follow-up procedures and risk factors.</p> <p>This is now reflected in the text in section4.1:</p>

		<p>following the comments, suggestions and proposed amendments of the professional breast care related societies and, in particular, of breast oncology surgeons who specialise in breast reconstruction, whose expert opinion we believe should be taken into consideration when making crucial decisions in this field.</p> <p>Europa Donna is the umbrella Coalition of 47 national breast cancer patient organisations. That means 47 different health care systems with huge differences in both access to treatment and surgical options and to information on best practice.</p> <p>Europa Donna advocates for the right of all European women to the best available treatment and surgical solutions. All European women should be given the opportunity to explore every alternative option of surgical breast reconstruction as appropriate for her specific clinical case.</p> <p>All European women should have the right to make informed decisions resulting from a shared pathway with a multidisciplinary professional team including pathologist, oncologist, surgeon, breast care nurse, etc.. All aspects of breast reconstruction should be evaluated and discussed with the patient, expressly including advantages, disadvantages, follow up procedures and risk factors.</p> <p>For technical aspects of breast implants and their safety, patients do not have the knowledge or the background to evaluate and choose a solution rather than another. For that type of decision, a patient would seek the learned opinion of and trust her medical team, with the understanding that preoperative clinical conditions, body type and shape, therapeutic options and related side effects and complications must guide the shared decision making pathway.</p> <p>In such perspective, we share our oncology surgeon experts' view in expecting that Institutions such as the SCHEER and other dedicated commissions around the world should (i) supervise surgical activity, in order to ensure that choices are not company-driven but taken exclusively for the advantage of patients and (ii) make sure that</p>	<p>“Some trends are apparent in the literature for the use of one or another type of breast implant. However, the clinical indications for the use of a specific type of breast implant should depend on a consultation between clinician and patient to allow informed decision making to take place with regard to the choice of an appropriate breast implant. For breast reconstruction, a shared consultation with a multidisciplinary healthcare team including a pathologist, oncologist, surgeon, breast care nurse, etc., should be held with the patient to allow informed decision making to take place with regard to the breast reconstruction procedure as well as the choice of implant. For both aesthetic and reconstructive surgery, all aspects of breast implants should be evaluated and discussed with the patient, expressly covering advantages, disadvantages, follow-up procedures and risk factors.”</p> <p>Regarding the supervision of surgical procedures and availability of medical devices, SCHEER has no role in these activities. SCHEER acts as an independent, scientific advisory body to the European Commission according to its published mandate.</p>
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			decisions regarding availability of medical devices such as breast implants, which are crucial for oncological surgery, be objective, evidence based and with the exclusive aim of safeguarding patients.	
5	Cerkes Nazim, ISAPS, International	ABSTRACT	<p>4. Practical</p>  <p>ISAPS_COMMENT_on_SCHEER_report_fin:</p> <p>In order to accommodate the individual clinical situation in each patient it is essential to emphasize the need for each surgeon on having a complete range of breast implants, for both breast augmentation and reconstruction. An eventual ban on all textured implants will prevent the use of anatomical implants which will have a big impact on the quality of outcomes as it is considered the gold standard in some patients particularly in reconstructive cases.</p> <p>In addition, the use of smooth round implants could cause further issues, from a cost-effectiveness and risk-benefit point of view. More complication will necessitate more re-operations and this with less individualized results and less satisfied patients. The suggestion that reconstruction with autologous tissues is the solution is not acceptable for all the surgeons and not applicable to all patients (no long-term evidence, high costs, long surgical sessions, more procedures, etc.)</p> <p>Conclusion Aesthetic plastic surgeons are very much aware of the responsibility they carry when serious or even possibly life-threatening disease can appear as the result of an aesthetic procedure. They use a professional, evidence-based approach towards BIA-ALCL and take this condition (along with Breast Implant Illness) very seriously. We understand that the SCHEER report holds a big responsibility towards not only all patients but to the plastic surgery community too. Involvement of all relevant parties when drawing up such a report should be mandatory. The current report can be viewed as misleading as it suggests that</p>	<p>SCHEER agrees with the comment raised that a variety of breast implants are available to suit a range of patients with a variety of clinical and aesthetic needs. In the abstract, the text concerning textured implants has been revised to reflect this; SCHEER has modified the statement on textured implants, as it is aware that there is a need for breast implants with a variety of surfaces.</p> <p>Modified text:</p> <p>“Overall SCHEER considers that there is a moderate weight of evidence for a causal relationship between textured breast implants and BIA-ALCL, particularly in relation to implants with an intermediate to high surface roughness.</p> <p>At this point it should be noted that i) there are several types of textured implants ii) surface textures of breast implants are not all manufactured in the same way, and iii) implants with diverse surface textures may also present different benefits. The magnitude of the risk per type of textured implant is difficult to establish due to the low incidence of the risk. Even with macro-textured implants, BIA-ALCL has a very low incidence. Therefore, risk assessments per implant type are needed. Furthermore, the risk should be weighed against the benefits. There is also a need for an unambiguous, clinically validated classification system for breast implants including more parameters than just “surface roughness”.; A history of textured breast implants/expanders appears to be necessary but not sufficient for the development of BIA-ALCL.”</p> <p>SCHEER is aware that the use of breast implants can be accompanied by complications. Regarding the use of the newer generation of smooth implants, there is some controversy in the literature regarding the number of complications that can occur compared to the use of</p>


			<p>removing all textured implants from the market will avoid this disease while totally neglecting the negative impact of such a decision on the quality of life of numerous pasts, present and future patients.</p> <p>We strongly advise and request a revision of this document before official publication. We would also be willing to enter formal discussions with the SCHEER Committee to try and shed further light on the number of issues we raised in this letter which we believe will both improve patient safety and result in better outcomes.</p>	<p>textured implants.</p> <p>Sforza M, Hammond DC, Botti G, Hedén P, Chacón Quirós M, Mendonça Munhoz A, Kinney BM, Corduff N. Expert Consensus on the Use of a New Bioengineered, Cell-Friendly, Smooth Surface Breast Implant. PMID: 30958549 PMCID: PMC6460429 DOI: 10.1093/asj/sjz054</p> <p>Sforza M, Zaccheddu R, Alleruzzo A, Seno A, Mileto D, Paganelli A, Sulaiman H, Payne M, Maurovich-Horvat L. Preliminary 3-Year Evaluation of Experience With SilkSurface and VelvetSurface Motiva Silicone Breast Implants: A Single-Center Experience With 5813 Consecutive Breast Augmentation Cases. Aesthet Surg J. 2018 May 15;38(suppl_2):S62-S73. doi: 10.1093/asj/sjx150. PMID: 29040364.</p> <p>SCHEER does not recommend removal of all textured implants from the market. Based on the evaluated evidence, SCHEER has concluded that there is a clear association between the occurrence of BIA-ALCL and the presence of macro-textured implants. This has now explicitly included in the text.</p> <p>Regarding the inclusion of types of studies, ‘reconstructive and/or aesthetic surgeries’ in the cited large scale reports, both types of implant procedures are represented in this SCHEER report.</p> <p>According to the information available to SCHEER, for most of the BIA-ALCL cases discussed in the cited references, an evaluation of implant history has been performed by the authors. In general, history of the use of both textured and smooth implants was noted.</p>
6	Cerkes Nazim, ISAPS,	ABSTRACT	<p>2. Prejudices The SCHEER report states that “the choice of implants does not depend</p>	<p>This has been addressed in the response to the first comment.</p>

<p>International</p>	<p>on the clinical condition, but instead “on the clinician’s and patient’s preferences, and consequently information provided by industry and/or media sources .” ISAPS disagrees with SCHEER’s statement that the influence of industry and media would prevail over the assessment of the surgeon when choosing a specific type of implant. On the contrary, it is our opinion that patient’s initial condition determines the best choice of implants for her specific expectation. We disagree with the comment of SCHEER regarding the fact that the “surgeon chooses implants not per clinical need.” There is a need for each surgeon in having a complete range of breast implants, both for breast augmentation and reconstruction.</p> <p>Social media and representatives from the industry do put pressure on our surgical specialty but suggesting that non-scientific influencers and industry determine our decisions is misleading, highly inaccurate and extremely offensive to the integrity of aesthetic plastic surgeons, not only in the European Union and UK, but in the world in general. The fact that National Aesthetic Plastic Surgery organizations were not pro-actively contacted is disappointing enough given the fact that the majority of breast implants are used for aesthetic purposes.</p> <p>There seems to be a clear prejudice against the use of all textured implants and the report focuses on reconstructive use of implants and hardly mentions the consequences for aesthetic indications. There has not been adequate discussion on the clinical situations where microtextured implants may have a role to play eg. tuberous breasts or breast footprints in which the vertical and horizontal lengths are quite different.</p> <p>3. Science The majority of the information presented in the SCHEER report is based on interpretation of referenced articles. Unfortunately, not all published papers are taken into account which limits the current epidemiological analysis. For proper analysis there is a need of well-designed data collection and the use of proper registries which has not been done by the Committee. The study is mostly based on reconstructive cases rather than aesthetic ones which are the vast</p>	<p>SCHEER agrees with this comment in that the choice of breast implant should not be driven by commercial aspects, but rather by the most appropriate implant for that specific patient with selection based on the most up-to-date scientific evidence available. Indeed, patients should be given the opportunity to explore all appropriate alternative options for surgical breast reconstruction. A shared consultation with a multidisciplinary healthcare team including a pathologist, oncologist, surgeon, breast care nurse, etc. should be held with the patient to allow informed decision making to take place with regards to the breast reconstruction procedure as well as the choice of implant. Indeed, all aspects of breast reconstruction should be evaluated and discussed with the patient, expressly covering advantages, disadvantages, follow-up procedures and risk factors.</p> <p>This is now reflected in the text in section 4.1:</p> <p>“Some trends are apparent in the literature for the use of one or another type of breast implant. However, the clinical indications for the use of a specific type of breast implant should depend on a consultation between clinician and patient to allow informed decision making to take place with regards to the choice of an appropriate breast implant. For breast reconstruction, a shared consultation with a multidisciplinary healthcare team including a pathologist, oncologist, surgeon, breast care nurse, etc. should be held with the patient to allow informed decision making to take place with regards to the breast reconstruction procedure as well as the choice of implant. For both aesthetic and reconstructive surgery, all aspects of breast implants should be evaluated and discussed with the patient, expressly covering advantages, disadvantages, follow-up procedures and risk factors.”</p>
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			<p>majority of cases where implants are used.</p> <p>According to the current literature, we cannot exclude that primary cases with smooth implants don't exist, in fact according to the FDA they do exist. Absence of evidence is not evidence of absence. A lot of emphasis is placed on the fact that some of the smooth cases had prior textured implants. However, no investigations have been done to check which of the textured cases had a smooth implant. Thus, there seems to be a bias towards textured implants. As to the surface, there is currently no clear definition of surface. There is a big difference between micro textured on one end and polyurethane on the other end of the spectrum. If we were to establish a new classification, it is advisable that it is based on clinical relevance. See also our specific comments in addendum to article 2.1</p>	
7	Cerkes Nazim, ISAPS, International	ABSTRACT	<p>As an international society, ISAPS represents more than 4,500 plastic surgeons with a focus on aesthetic plastic surgery of which more than 1,500 (33%) reside in the European Union and the UK. We both collaborate are in close contact with their National Societies of Aesthetic Plastic Surgery. In this capacity we have received numerous reactions to both the content and conclusions of the SCHEER report with requests to respond to various aspects in the document.</p> <p>Although ISAPS agrees and applauds most of the conclusions reached in the SCHEER report, it has some concerns regarding potential biases and the omission of important information that is essential to offer a more balanced overview of the possible emerging risk of BIA-ALCL.</p> <p>It's regrettable that the National Aesthetic Plastic Surgery Societies within the European Union and the UK were not consulted during the drafting of this document especially since the vast majority (75%) of breast implants are being used for aesthetic purposes as stated in your report. Thirdly, some of the conclusions reached in the SCHEER report are premature on a number of aspects:</p> <ol style="list-style-type: none"> <li>1. Risk Assessment and Ethics</li> <li>2. It holds prejudices</li> <li>3. Scientifically incomplete</li> </ol>	<p>After the mandate was accepted by SCHEER, an open call for participation and information was published, followed by a public consultation after publication of the Preliminary Opinion.</p> <p>Regarding participation in the drafting process of this Opinion, SCHEER has the following comments:</p> <p>Expert selection was performed according to the Rules of procedures of the Scientific Committees (<a href="https://ec.europa.eu/health/scientific_committees/docs/rules_procedure_2016_en.pdf">https://ec.europa.eu/health/scientific_committees/docs/rules_procedure_2016_en.pdf</a>).</p> <p>There was a public, open call for experts to participate in the respective working group formed by SCHEER (<a href="https://ec.europa.eu/health/scientific_committees/call_experts/call_experts_bia_alcl_en">https://ec.europa.eu/health/scientific_committees/call_experts/call_experts_bia_alcl_en</a>), the deadline of which was actually extended once (from December 4th, 2019 to January 3rd, 2020) due to the low response received from experts. However, all experts and their respective societies have had the opportunity to contribute towards the finalisation of this Opinion during the public consultation period,</p>



		<p>4. Practical consequences</p> <p>1. Risk Assessment and Ethics The fact that BIA-ALCL is considered as an emerging risk that warrants a report is not challenged. BIA-ALCL is a very rare disease that can be treated and cured if recognized early. The stable increase of this disease must be closely monitored. The Aesthetic Plastic Surgery community is very aware of this and yearly follow-up is universally adopted as the benchmark now. Registration of all implants in device registries is strongly recommended to be able to detect rare diseases early and enable scientific research for improved follow-up possible. This holds true for monitoring all types of implants and all related diseases, not just breast-implants.</p> <p>The suggestion of this report to ban all textured implants due to the low but real risk of BIA-ALCL would unleash a serious number of problems - both medical and social- in the community:</p> <ol style="list-style-type: none"> <li>1. anxiety and unrest amongst patients with breast implants and those contemplating breast reconstruction or augmentation surgery</li> <li>2. unnecessary revisional operations with significant complications which would hugely outnumber the very few cases of BIA-ALCL that would be avoided with this measure</li> <li>3. the enormous financial burden placed on governments to both subsidize these revisional operations</li> <li>4. the significant expenditure required for governments to communicate widely to the public via the various media channels on educating them on the conclusions of the SCHEER report</li> <li>5. the serious harm to the reputation of plastic surgeons in their ability to provide quality care for patients needing future breast reconstructions and augmentations.</li> <li>6. There was no mention in the report that around 75% of aesthetic primary augmentations in Australia and New Zealand that developed BIA-ALCL were performed by non-specialist surgeons i.e. they were doctors or general practitioners masquerading as 'cosmetic surgeons'. Perhaps governments have an opportunity here to focus on better regulating the cosmetic surgery industry and protecting the public from</li> </ol>	<p>and they did so, by providing numerous comments as detailed in this document.</p> <p>So, there has been ample opportunity for the public including scientific societies to provide information and comments and in doing so, to contribute to the SCHEER report.</p>
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			so called fraudsters.	
8	Parreira Carlos, EASAPS and ESAPS, Belgium	ABSTRACT	<p>Line 19:  “and is mainly associated with textured implants.”  Please change this to:  “and is mainly associated with Biocell textured implants.”</p> <p>Also line 29-30  “There are several alternatives to breast implants that involve plastic surgery techniques, either using autologous flap tissue or autologous fat transfer. “  This is a bit limited. please correct to:  “For aesthetic patients the alternatives are limited to autologous fat transfer. Unfortunately, this technique is only applicable in limited cases with low predictability. There are other alternatives to breast implants in reconstructive surgery that involve either using autologous flap tissue or autologous fat transfer. “</p>	<p>Addressed in the text of the opinion that is now indicated with “macro-textured”.</p> <p>SCHEER agrees with this comment and has adapted the text accordingly.</p> <p>Modified text:  “However, individual patient characteristics may limit the application of these techniques.”</p>
9	D'andrea francesco, Italian society of Plastic Surgery SICPRE, Italy	ABSTRACT	<p>Critical considerations on the document</p>  <p>Scientific_Committee_on_Health.docx</p> <p>The Italian Society of Reconstructive, Regenerative and Aesthetic Plastic Surgery (S.I.C.P.R.E.) represented in this document by its President, Prof. Francesco D'Andrea, and all the members of the Board of Directors wishes to represent some critical considerations on this document.</p> <ul style="list-style-type: none"> <li>• On anatomical implants with a textured surface vs. round implants with a smooth surface</li> </ul> <p>First of all, we would like to underline the importance of anatomical implants both in aesthetic surgery and reconstructive surgery, for the maintenance or restoration of the shape of the udder. By definition, there are no anatomical implants with a smooth surface that could not adhere to the tissues and would inevitably undergo rotation or dislocation.</p> <p>Mostly interesting is an optimal dimensional correction, by correcting</p>	<p>This comment has been addressed in response to the comments above.</p> <p>Modified text:  “Overall SCHEER considers that there is a moderate weight of evidence for a causal relationship between textured breast implants and BIA-ALCL, particularly in relation to implants with an intermediate to high surface roughness.</p> <p>At this point it should be noted that i) there are several types of textured implants ii) surface textures of breast implants are not all manufactured in the same way, and iii) implants with diverse surface textures may also present different benefits. The magnitude of the risk per type of textured implant is difficult to establish due to the low incidence of the risk. Even with macro-textured implants, BIA-ALCL has a very low incidence. Therefore, risk assessments per implant type are needed. Furthermore, the risk should be weighed against the</p>

		<p>or reconstructing a shape more than a volume. The anatomical prostheses, with textured surface, stable shape and cohesive silicone, guarantee a three-dimensional correction allowing an optimal increase in volume in aesthetic surgery and a precise reconstruction of the shape in reconstructive surgery. The anatomical implants - varying in the three basic dimensions height and projection, independently of volume, guarantee an optimal correction/reconstruction of the udder, unlike round implants which, characterised only by two dimensions (diameter and projection), are able to integrate volumes but modify or recreate the shape in a non-significant way. More predictable results can be obtained better and consistently with anatomically shaped implants than with round ones . Improved results with smooth prostheses can be achieved by combining or following up other procedures, such as lipofilling, which involve additional costs and risks and less predictability in reconstructive surgery and remodelling breast surgery (tuberous breast, s. of Poland).</p> <p>There are papers in literature that describe very precise algorithms for the exact selection of anatomical implants, for the correction, restoration and integration of mammary cones (Tebbets, Nava, Montemurro, Mallucci).</p> <p>Tebbets, John B. MD "A system for breast implant selection based on patient tissue characteristic and implant-soft tissue dynamics", P.R.S. april 1, 2002</p> <p>Tebbets, John B. MD " Achieving a zero percent reoperation rate at 3 years in a 50 consecutive case augmentation mammoplasty premarket approval study", P.R.S. 2006 nov</p> <p>Tebbets, John B. MD " Five critical decision in breast augmentation using five measurements in 5 minutes: the high five decision support process", P.R.S. 116, 2005</p> <p>Patrick Mallucci et al."Design for natural breast augmentation: the ICE principle", P.R.S. 2016 jun</p> <p>Per Heden, Paolo Montemurro et al. "Implementation of the akademikliniken method of subpectoral breast augmentation with anatomic, highly cohesive silicone gel implants: the first 620 consecutive cases", P.R.S. global open, 2016 sept.</p>	<p>benefits. There is also a need for an unambiguous, clinically validated classification system for breast implants including more parameters than just “surface roughness”. A history of textured breast implants/expanders appears to be necessary but not sufficient for the development of BIA-ALCL.”</p> <p>The choice of implant is not addressed in the abstract and therefore these comments do not apply.</p> <p>SCHEER acknowledges that a number of papers have been published describing methods for the selection of anatomical or round implants but this is out of the scope and mission of the mandate given to SCHEER and is therefore not addressed in this report.</p>
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10	<p>Mercer Nigel, Plastic, Reconstructive and Aesthetic Expert Advisory group, United Kingdom</p>	<p>ABSTRACT</p>	<p>P2: The incidence of BIA-ALCL is considered low, varies by implant type, and is mainly associated with textured implants. Overall there is a moderate level of evidence for a causal relationship between 23 textured breast implants and ALCL</p> <p>P2 Line 17: safe margin – The safe margin needs to be defined.</p> <p>P2 L29-30: there are several alternatives to implants: If this statement is made it needs to be qualified because this applies only in certain circumstances. The document should specify what those options are for both reconstructive and aesthetic cases. For each indication, it needs stated to whom they are applicable and what the associated pros and cons of the procedures are. This is expanded later in the document but not well.</p>	<p>The text has been changed in the abstract to reflect this comment.</p> <p>Modified text:</p> <p>“Overall SCHEER considers that there is a moderate weight of evidence for a causal relationship between textured breast implants and BIA-ALCL, particularly in relation to implants with an intermediate to high surface roughness.</p> <p>At this point it should be noted that i) there are several types of textured implants ii) surface textures of breast implants are not all manufactured in the same way, and iii) implants with diverse surface textures may also present different benefits. The magnitude of the risk per type of textured implant is difficult to establish due to the low incidence of the risk. Even with macro-textured implants, BIA-ALCL has a very low incidence. Therefore, risk assessments per implant type are needed. Furthermore, the risk should be weighed against the benefits. There is also a need for an unambiguous, clinically validated classification system for breast implants including more parameters than just “surface roughness”. A history of textured breast implants/expanders appears to be necessary but not sufficient for the development of BIA-ALCL.”</p>

				<p>The main subject of the Opinion is the possible relationship of BIA-ALCL and breast implants. Information regarding techniques used for breast augmentation surgery and types of implants available is provided purely as background information and therefore is not extensively discussed in the report.</p>
11	parreira José Carlos, E(A)SAPS, Portugal	ABSTRACT	<p>Comments of E(A)SAPS on Scheer Report</p> <div style="display: flex; justify-content: space-around; align-items: center;"> <div style="text-align: center;">         SCHEER_E_A_SAPS_comments_03.12.docx     </div> <div style="text-align: center;">         SCHEER_letter_03.12.20.docx     </div> </div>	<p>Regarding participation in the drafting process of this Opinion, SCHEER has following comments. Expert selection was performed according to the Rules of procedures of the Scientific Committees (<a href="https://ec.europa.eu/health/scientific_committees/docs/rules_procedure_2016_en.pdf">https://ec.europa.eu/health/scientific_committees/docs/rules_procedure_2016_en.pdf</a>).</p> <p>There was a public, open call for experts to participate in the respective working group formed by SCHEER (<a href="https://ec.europa.eu/health/scientific_committees/call_experts/call_experts_bia_alcl_en">https://ec.europa.eu/health/scientific_committees/call_experts/call_experts_bia_alcl_en</a>), the deadline of which was actually extended once (from December 4th, 2019 to January 3rd, 2020) due to the low response received from experts. However, all experts and their respective societies have had the opportunity to contribute towards the finalization of this Opinion during the public consultation period, and they did so by providing numerous comments, as detailed in this document.</p> <p>So, there has been ample opportunity for the public including scientific societies to provide information and comments and in doing so, to contribute to the SCHEER report.</p> <p>Some of the other comments listed in these documents are not in reference to the abstract but to the main body of the text and will therefore be addressed later.</p>

12	CAMPANALE ANTONELLA, ITALIAN MINISTRY OF HEALTH, Italy	ABSTRACT	<p>p.2 line 9-12: The IMoH published two original articles and one letter on the Plastic Reconstructive Surgery Journal (one of the most important Journal in Plastic Surgery) between 2018 and 2020 but none of these articles has been considered relevant by the WG. As this is the first time that an Independent Institution contributes with scientific papers to the research on the BIA-ALCL issue, we would like to Know the reasons that drove the Authors considering our works not relevant. See: Campanale et al, 2020; Campanale et al 2018 (a); Campanale et al 2018 (b)</p> <p>p.2 line 18-19: To date all studies in literature refer to the implant at the time of the diagnosis, and a lot of the data regarding clinical and implant history are declared as missing. We demonstrated in our paper (Campanale et al.2020) that this is a wrong approach in the effort of identifying the involved device. It is important to look at the device implanted at the onset of the first symptoms. Authors need to recover and review the clinical history of all their reported cases. Otherwise any effort to come to right conclusion relative to the involved devices will be wasted. This sentence should be modified as “The incidence of BIA-ALCL is considered low and varies by implant type”, deleting the reference to textured implants.</p> <p>p. 2 line 19-22: We agree that using the sales data alone can represent a limitation, but complete them with data obtained from vigilance and surveillance activities on National Health Care System can represent a strength point. Indeed in Campanale et al 2018 (a); Campanale et al 2018 (b), the IMoH explained how the denominator has been estimated showing the above-mentioned approach. To date the estimated incidence worldwide still has a significant variability but everybody knows that this variability is attributable to all the factors that influence the numerator and the denominator in each country. We are convinced that the only way to achieve a reliable value in the numerator, is through the CONSTANTLY PROMOTED awareness of both physicians and patients. The variables used to estimate the denominator were: the number of prostheses implanted per year, the number of prostheses</p>	<p>Not all the comments made here are relevant to the abstract, as they refer to literature citations: they will therefore be addressed later.</p> <p>The literature presented in the comment was considered by SCHEER using the WoE approach and are mentioned in the accompanying excel file.</p>

			<p>implanted with aesthetic and reconstructive purposes and the mean lifetime of the implant. This is very important because these devices DO have a limited lifetime. These variables have been obtained working with the distributors of breast implants and according to the results of surveillance activities on our healthcare system. DUE TO OUR WORK, WE FEEL CONFIDENT THAT our incidence is rather reliable but knowing the limits of our studies we are aware that only BY establishing a mandatory breast implant registry we will have a more realistic BIA-ALCL incidence.</p> <p>p. 2 line 23-24: We would like to understand how the WG has evaluated the level of evidence as MODERATE. Moreover, we would like to know the scientific evidence that induced the WG to state that there is a “causal relationship” between textured breast implants and ALCL. We believe that the association found and showed in Literature should not be misunderstood as a causal relationship.</p> <p>References:  Campanale 2020: The Crucial Role of Surgical Treatment in BIA-ALCL Prognosis in Early- and Advanced-Stage Patients. <i>Plast Reconstr Surg.</i> 2020 Nov;146(5):530e-538e.  Campanale 2018 (a): 22 Cases of Breast Implant-Associated ALCL: Awareness and Outcome Tracking from the Italian Ministry of Health. <i>Plast Reconstr Surg.</i> 2018 Jan;141(1):11e-19e.  Campanale 2020 (b):Reply: 22 Cases of Breast Implant-Associated ALCL: Awareness and Outcome Tracking from the Italian Ministry of Health. <i>Plast Reconstr Surg.</i> 2018 May;141(5):779e.</p>		<p>These papers describe case reports and as such, do not fulfil the selection criteria of the literature search as stated by the SCHEER WG. Additionally, one of these papers was published outside of the search period and therefore cannot be included in the report. The paper of 2020 has been considered and has now been cited.</p>
13	Parreira Carlos, EASAPS and ESAPS, Belgium	ACKNOWLEDGMENTS	<p>The present SCHEER report 2020 has not included the point of view and opinion of AESTHETIC plastic surgeons and their organizations EASAPS / ESAPS and ISAPS. EASAPS, the European Association of Societies of Aesthetic Plastic Surgery and ESAPS, the European Society of Aesthetic Plastic Surgery are jointly referred to as E(A)SAPS. E(A)SAPS represents individual aesthetic plastic surgeons from 52 European countries and their National Aesthetic Plastic Surgery Societies. The task force “ALCL in Europe” has been investigating the occurrence of confirmed cases of BIA-ALCL and deaths across Europe on a bi-annual basis, since 2017.</p>		<p>Regarding participation in the drafting process of this Opinion, SCHEER has the following comments: Expert selection was performed according to the Rules of procedures of the Scientific Committees (<a href="https://ec.europa.eu/health/scientific_committees/docs/rules_procedure_2016_en.pdf">https://ec.europa.eu/health/scientific_committees/docs/rules_procedure_2016_en.pdf</a>). There was a public, open call for experts to participate in the respective working group formed by SCHEER (<a href="https://ec.europa.eu/health/scientific_committees/call_experts/call_experts_bia_alcl_en">https://ec.europa.eu/health/scientific_committees/call_experts/call_experts_bia_alcl_en</a>), the deadline of which was actually extended once (from December 4th, 2019 to January 3rd, 2020) due to the low</p>


			Actual data is conveyed via newsletters, websites and modern social media to European aesthetic plastic surgeons. E(A)SAPS interacts with the international notifying bodies as well as with the National Societies. It is regrettable that representative organizations were not contacted while members of these organizations have extensive experience in writing such documents while drafting European Standard EN 16703 Aesthetic Surgery Services. The current list of experts is NOT representative of all current experts on this topic.	<p>response received from experts. However, all experts and their respective societies have had the opportunity to contribute towards the finalisation of this Opinion during the public consultation period, and they did so, by providing numerous comments as detailed in this document.</p> <p>So, there has been ample opportunity for the public including scientific societies to provide information and comments and in doing so, to contribute to the SCHEER report.</p>
14	Garson Sebastien, SNCPRE, France	ACKNOWLEDGMENTS	Please report the conflict of interest of the expert, two of the clinical experts get COI actual or in the past with breast implant factory. Please choose better one next time.	Before participating in any WG of the SCHEER, the interests of members must be declared and then it is up to the SCHEER to decide whether these declarations constitute a Conflict of Interest. All interests of the participating WG members are publicly available on the website of the EC.
15	De Mezerville Roberto, Establishment Labs, Costa Rica	1. MANDATE FROM THE EU COMMISSION SERVICES	<p>COMMENT: the committee refers to Anatomical implants as “textured in some way”.</p> <p>RECOMMENDATIONS: In addition to round textured implants, anatomically shaped implants are textured in the same way (per manufacturer process).</p> <p>Moreover, the committee is not recognizing the fact that there is a commercially available alternative of a smooth surface anatomical implants, which has CE Mark.</p>	<p>The Mandate of the Commission is an officially published EU document and as such cannot be modified.</p> <p>However, the SCHEER recognizes that an anatomical implant is not synonymous with textured implant. This has now been addressed in the text of the Opinion. The word “rarity” has been replaced by uncommon nature” where appropriate.</p> <p>NOTE: “rarity” is only used in the Mandate.</p>
16	Cardoso Maria-Joao, Eusoma (European Society of Breast Cancer Specialists), Italy	1. MANDATE FROM THE EU COMMISSION SERVICES	page 6 lines 6;8;39	The Mandate of the Commission is an officially published EU document and as such cannot be modified.
17	Mercer Nigel, Plastic, Reconstructive and Aesthetic Expert Advisory	1. MANDATE FROM THE EU COMMISSION SERVICES	P7 Line 28: ‘Uncommon nature’ would be more appropriate than ‘rarity’.	<p>The Mandate of the Commission is an officially published EU document and as such cannot be modified.</p> <p>We agree that ‘uncommon’ is more appropriate and have updated the</p>

	Group, United Kingdom	ON SERVICES		text of the Opinion.
18	Mercer Nigel, Plastic, Reconstructive and Aesthetic Expert Advisory Group, United Kingdom	1. MANDATE FROM THE EU COMMISSION SERVICES	<p>P6 Line 1: “Breast implant associated anaplastic large cell lymphoma (BIA-ALCL) is a rare sub type of 6 non-Hodgkin's lymphoma”. There is inconsistency in terms throughout the document. It is more scientific and legally valid to use ‘uncommon’.</p> <p>P6 Line 19-23: Should state 'cumulative cases', otherwise it gives the impression those were the reports for that single year.</p> <p>P6 Line 23: presumably MHRA is one of the EU competent authorities?</p> <p>P6 Line 45: Anatomically shaped implants are commonly textured in some way: ‘Usually’ would be better than ‘commonly’.</p> <p>P7 line 5-6: We are agreed that a better system of classification of the surface is required (one that reflects that ‘smooth’ is not smooth at the microscopic level). A world-wide standardised classification of implant surface roughness is required. The current ISO classification is out of date.</p>	<p>The Mandate of the Commission is an officially published EU document and as such cannot be modified.</p> <p>Some of the other comments will be addressed in the main body of the text of the Opinion.</p>
19	CAMPANALE ANTONELLA, ITALIAN MINISTRY OF HEALTH, Italy	1. MANDATE FROM THE EU COMMISSION SERVICES	<p>p.6 line 24-25: This sentence is detrimental because nobody can still link the lymphoma with textured devices considering that the reported cases can be wrongly referred to the implant at the time of diagnosis. The implant history is critical to understand the right involved implant. In Campanale 2020, the IMoH has highlighted the importance of recovering the complete data and information related to each device if an implant history exists. Each case must be accurately studied in order to understand when the first symptoms occurred and which was the device implanted at the onset of these symptoms.</p> <p>p.6 line 25-26: The amount of missing data represents a relevant bias of the research in this field. This lack of information prevents to achieve strong scientific evidences about the association of any type of implant surface with the development of the BIA-ALCL disease.</p> <p>p. 6 line 37-40: It is unfair and speculative to recall the importance of a</p>	<p>The Mandate of the Commission is an officially published EU document and as such cannot be modified.</p> <p>As a rule, it is a good and general practice for the implant history of BIA-ALCL cases to be considered and reported to the relevant authorities to allow them to keep records of implant use and BIA-ALCL incidence.</p> <p>According to the information available to SCHEER, for most of the BIA-ALCL cases discussed in the cited references, an evaluation of implant history has been performed by the authors. In general, history of the use of both textured and smooth implants was noted.</p>




			<p>previous implant history only when a smooth device has been found at the time of diagnosis. We want to stress the following concept: the implant history is ALWAYS critical, independently from the device implanted at the time of diagnosis.</p> <p>p.7 line 2-5: The WG is referring to the historical advantages introduced by the textured surfaced implant and this concept is cited in paragraph 4.2 TYPES OF BREAST IMPLANTS page 14 line 47-48 as well. The references related to these advantages would be added. The rate of capsular contractures, implant ruptures or other events related to smooth implants need to be accounted when patients are addressed to use smooth implants.</p> <p>p. 7 line 21-24: This is a correct sentence that is in contradictions with sentences at page 2 line 23-24 and conclusions at p. 9 line 1-2: “Based on a moderate weight of evidence, the SCHEER concludes that there is a causal relationship between textured breast implants and BIA-ALCL”</p> <p>p. 8 line 30-31: The IMoH would like to underline that most of the published studies on the BIA-ALCL are low evidence studies (IV to VII level of evidence), thus the above sentence must be considered wrong and we wonder what is the moderate scientific evidence that WG is talking about when they state that there is a “causal relationship” between textured breast implants and ALCL. Once more, we do believe that the WG should not be misunderstood the association found and showed in Literature with the causal relationship.</p> <p>p. 8 line 45-48: We all agree that there is a chronic inflammation that plays a central role in the development of BIA-ALCL but the breast implant alone is not sufficient to cause this chronic inflammation, otherwise we should have a much higher number of BIA-ALCL cases in the last 10 years. Moreover, there still needs to understand why with the same device only very few patients develop this disease.</p>	
20	BENITO-RUIZ JESUS, ANTIAGING	1. MANDATE FROM THE	<p>Line 46 and 47.  Comment: The selection of implants are based on breast (fingerprint of the breast, shape, ptosis) and chest characteristics. The diagnosis</p>	The Mandate of the Commission is an officially published EU document and as such cannot be modified.


	GROUP BARCELONA, Spain	EU COMMISSIO ON SERVICES	(breast absence, amastia, tuberous breast and even in pure aesthetic cases for changes of volume and shape) is paramount to choose the proper implant (shape and volume). The final decision is clinical judgment first. This is matched with patient desires as much as possible. This is key to prevent complications such as waterfall deformity, rippling, double fold, dynamic breast, etc.	<p>Factors influencing the selection of implants have been discussed above and will be modified in the main body text of the Opinion.</p> <p>SCHEER agrees with this comment in that the choice of breast implant should not be driven by commercial aspects, but rather by the most appropriate implant for that specific patient with selection based on the most up-to-date scientific evidence available. Indeed, patients should be given the opportunity to explore all appropriate alternative options for surgical breast reconstruction. A shared consultation with a multidisciplinary healthcare team including a pathologist, oncologist, surgeon, breast care nurse, etc should be held with the patient to allow informed decision making to take place with regards to the breast reconstruction procedure as well as the choice of implant. Indeed, all aspects of breast reconstruction should be evaluated and discussed with the patient, expressly covering advantages, disadvantages, follow-up procedures and risk factors.</p> <p>This is now reflected in the text in section 4.1.</p> <p>“Some trends are apparent in the literature for the use of one or another type of breast implant. However, the clinical indications for the use of a specific type of breast implant should depend on a consultation between clinician and patient to allow informed decision making to take place with regards to the choice of an appropriate breast implant. For breast reconstruction, a shared consultation with a multidisciplinary healthcare team including a pathologist, oncologist, surgeon, breast care nurse, etc. should be held with the patient to allow informed decision making to take place with regards to the breast reconstruction procedure as well as the choice of implant. For both aesthetic and reconstructive surgery, all aspects of breast implants should be evaluated and discussed with the patient, expressly covering advantages, disadvantages, follow-up procedures and risk factors.”</p>
21	Geertsma Robert, RIVM - National	2. CONCLUSI	2. Conclusions, p.8 , lines 30-31 and p.9 , lines 1-2 Statements on a moderate level of evidence for a causal relationship	SCHEER agrees.

	Institute for Public Health and the Environment, Netherlands	ONS	<p>between textured breast implants and ALCL imply that a causal relationship exists between ALCL and all types of textured implants. As can be concluded from multiple statements in the body of the Opinion, stratification between the relative risks of various types of textures (including no texture) is currently not possible. In order to provide an honest and complete picture of current knowledge, this should be explained carefully in the Opinion, and certainly also in the Conclusion, which is likely to undergo a much broader dissemination than the entire report. Furthermore, it is important also to point out that implants with different surface textures may also have different benefits, so in order to draw conclusions, a full benefit-risk evaluation should be made.</p> <p>In relation to this, SCHEER should consider including a statement in the Conclusion on the need for an unambiguous, uniform classification of different surface textures with more parameters than just “surface roughness”.</p>	<p>Text modified:</p> <p>“Based on these data SCHEER considers that there is a moderate weight of evidence for a causal relationship between textured breast implants and BIA-ALCL, particularly in relation to implants with an intermediate to high surface roughness.</p> <p>At this point it should be noted that i) there are several types of textured implants ii) surface textures of breast implants are not all manufactured in the same way, and iii) implants with diverse surface textures may also present different benefits. The magnitude of the risk per type of textured implant is difficult to establish due to the low incidence of the risk. Even with macro-textured implants, BIA-ALCL has a very low incidence. Therefore, risk assessments per implant type are needed. Furthermore, the risk should be weighed against the benefits. There is also a need for an unambiguous, clinically validated classification system for breast implants including more parameters than just “surface roughness”. A history of textured breast implants/expanders appears to be necessary but not sufficient for the development of BIA-ALCL.”</p>
22	Govrin Jacky, Beit Harofim Clinics	2. CONCLUSIONS	<p>N/A</p>  <p>Jacky_Govrin_response_to_SCHEER_prelim</p>	<p>SCHEER is providing a risk assessment; it is not promoting the ban of certain types of breast implants. The comment regarding the statement on textured implants has been modified in the text of the Opinion.</p> <p>Text modified:</p> <p>“Based on these data SCHEER considers that there is a moderate weight of evidence for a causal relationship between textured breast implants and BIA-ALCL, particularly in relation to implants with an intermediate to high surface roughness.</p>

				<p>At this point it should be noted that i) there are several types of textured implants ii) surface textures of breast implants are not all manufactured in the same way, and iii) implants with diverse surface textures may also present different benefits. The magnitude of the risk per type of textured implant is difficult to establish due to the low incidence of the risk. Even with macro-textured implants, BIA-ALCL has a very low incidence. Therefore, risk assessments per implant type are needed. Furthermore, the risk should be weighed against the benefits. There is also a need for an unambiguous, clinically validated classification system for breast implants including more parameters than just “surface roughness”.; A history of textured breast implants/expanders appears to be necessary but not sufficient for the development of BIA-ALCL.”</p>
23	No agreement to disclose personal data	2. CONCLUSIONS	<p>Page 8, line 30-31 ‘There is a moderate level of evidence for a causal relationship between textured breast implants and ALCL.’ Footnote 8: ‘Moderate weight of evidence: good evidence from a primary line of evidence but evidence from several other lines is missing (important data gaps) (see SCHEER WoE, 2018)’.</p> <p>Does the SCHEER find that there is a moderate level of evidence for a causal relationship between all textured breast implants and ALCL or does the level of evidence available vary based on specific aspects of the breast implant surface texture of textured implants?</p> <p>Have SCHEER considered IARC categories of evaluation with respect to agents which may be cancer causing in humans, for the assessment of the relationship between breast implants and BIA-ALCL?</p>	<p>Based on the available assessed literature, SCHEER has concluded that there is a moderate weight of evidence for a relationship between macro textured implants and BIA-ALCL. SCHEER is aware that not all types of textured implants are clearly associated with BIA-ALCL and has modified the text on textured implants accordingly.</p> <p>Text modified:</p> <p>“Based on these data SCHEER considers that there is a moderate weight of evidence for a causal relationship between textured breast implants and BIA-ALCL, particularly in relation to implants with an intermediate to high surface roughness.</p> <p>At this point it should be noted that i) there are several types of textured implants ii) surface textures of breast implants are not all manufactured in the same way, and iii) implants with diverse surface textures may also present different benefits. The magnitude of the risk per type of textured implant is difficult to establish due to the low incidence of the risk. Even with macro-textured implants, BIA-ALCL has a very low incidence. Therefore, risk assessments per implant type are needed. Furthermore, the risk should be weighed against the</p>

				benefits. There is also a need for an unambiguous, clinically validated classification system for breast implants including more parameters than just “surface roughness”.; A history of textured breast implants/expanders appears to be necessary but not sufficient for the development of BIA-ALCL.”
24	Clerico Luana, POLYTECH Health & Aesthetics, Germany	2. CONCLUSIONS	<p>"Based on a moderate weight of evidence, the SCHEER concludes that there is a causal relationship between textured breast implants and BIA-ALCL".</p>  <p>Clerico_commentary_to_Scheer_opinion.pdf</p> <p>Abstract - Lines 22/23 pag. 2; 2. Conclusions - Lines 30/31 pag. 8, and 1/2 pag. 9; 2.1 Answers to the Terms of References - Lines 22/23 pag 10.</p>	<p>SCHEER considers that as almost all implants, as far as identified in BIA-ALCL cases, are textured; in our opinion, this is a sufficient reason to use the term causal relationship. However, in the final Opinion, it is also now stated that in view of the uncommon occurrence of BIA-ALCL, it is clear that not all textured implants may result in BIA-ALCL.</p> <p>SCHEER does not promote the ban of textured implants and has adapted the text regarding the surface texture, i.e. the texture of surface implants.</p> <p>Text modified:</p> <p>“Based on these data SCHEER considers that there is a moderate weight of evidence for a causal relationship between textured breast implants and BIA-ALCL, particularly in relation to implants with an intermediate to high surface roughness.</p> <p>At this point it should be noted that i) there are several types of textured implants ii) surface textures of breast implants are not all manufactured in the same way, and iii) implants with diverse surface textures may also present different benefits. The magnitude of the risk per type of textured implant is difficult to establish due to the low incidence of the risk. Even with macro-textured implants, BIA-ALCL has a very low incidence. Therefore, risk assessments per implant type are needed. Furthermore, the risk should be weighed against the benefits. There is also a need for an unambiguous, clinically validated classification system for breast implants including more parameters</p>


				than just “surface roughness”. A history of textured breast implants/expanders appears to be necessary but not sufficient for the development of BIA-ALCL.
25	Parreira Carlos, EASAPS ESAPS, Belgium	2. CONCLUSIONS	<p>The collaborators of the SCHEER report must be commended for their efforts to describe the relation between ALCL and breast implants. It is regrettable however that the viewpoints of aesthetic plastic surgeons are not taken sufficiently into account. In our opinion, epidemiology and incidence rates for BIA-ALCL should not be exclusively based on two populations. The suggestion in the current report that removing all textured implants would be the solution is misleading. The different types of texturization cannot all be held accountable to the same degree of association with ALCL, especially since the main contributor (biocell) now has been withdrawn from the market. This same conclusion, once published, can be misinterpreted by the general press causing unnecessary worry among patients resulting in revision requests with possible complications which will hugely outnumber the prevention of ALCL-cases.</p> <p>We would like to add the following recommendations:</p> <ul style="list-style-type: none"> <li>• Manufacturers should provide information on European sales data during the last 10 years.</li> <li>• Reporting BIA-ALCL cases should be mandatory for all clinical institutions. Up and running breast implant registries should capture these cases.</li> <li>• Consensus guidelines for patients with textured implants who wish to remove them are needed.</li> <li>• A central European laboratory with main focus on future research with respect to BIA-ALCL histopathology and genetics is recommended.</li> </ul> <p>E(A)SAPS asks for an urgent revision taking the above remarks into account. We are always willing to collaborate and contribute to a next version of this report to improve patient safety in the future. Specifically to this paragraph we have the following comment: It is stated in line 33:</p>	<p>Regarding participation in the drafting process of this Opinion, SCHEER has the following comments: Expert selection was performed according to the Rules of procedures of the Scientific Committees (<a href="https://ec.europa.eu/health/scientific_committees/docs/rules_procedure_2016_en.pdf">https://ec.europa.eu/health/scientific_committees/docs/rules_procedure_2016_en.pdf</a>). There was a public, open call for experts to participate in the respective working group formed by SCHEER (<a href="https://ec.europa.eu/health/scientific_committees/call_experts/call_experts_bia_alcl_en">https://ec.europa.eu/health/scientific_committees/call_experts/call_experts_bia_alcl_en</a>), the deadline of which was actually extended once (from December 4th, 2019 to January 3rd, 2020) due to the low response received from experts. However, all experts and their respective societies have had the opportunity to contribute towards the finalisation of this Opinion during the public consultation period, and they did so by providing numerous comments, as detailed in this document.</p> <p>So, there has been ample opportunity for the public including scientific societies to provide information and comments and in doing so, to contribute to the SCHEER report.</p> <p>Based on the available data, SCHEER concluded that there is a causal relationship between BIA-ALCL and textured breast implants. However, in the final Opinion, it is also now stated that in view of the uncommon occurrence of BIA-ALCL, it is clear that not all textured implants may result in BIA-ALCL. It should be noted that a history of textured breast implants/expanders appears to be necessary but not sufficient for the development of BIA-ALCL.</p>

			<p>“The common factor underlying the occurrence of BIA-ALCL is the presence of a textured breast implant. “</p> <p>Better is:</p> <p>“The common factor underlying the occurrence of BIA-ALCL is the presence of a Biocell textured breast implant. “</p>	<p>Text modified:</p> <p>“Based on these data SCHEER considers that there is a moderate weight of evidence for a causal relationship between textured breast implants and BIA-ALCL, particularly in relation to implants with an intermediate to high surface roughness.</p> <p>At this point it should be noted that i) there are several types of textured implants ii) surface textures of breast implants are not all manufactured in the same way, and iii) implants with diverse surface textures may also present different benefits. The magnitude of the risk per type of textured implant is difficult to establish due to the low incidence of the risk. Even with macro-textured implants, BIA-ALCL has a very low incidence. Therefore, risk assessments per implant type are needed. Furthermore, the risk should be weighed against the benefits. There is also a need for an unambiguous, clinically validated classification system for breast implants including more parameters than just “surface roughness”.; A history of textured breast implants/expanders appears to be necessary but not sufficient for the development of BIA-ALCL.”</p> <p>Based on epidemiology, the text of the conclusion in section 6 was expanded by the addition of this sentence.</p> <p>“As far as the manufacturer was known most cases were found for the Biocell implant (textured by salt loss technique), while for PU coated breast implants BIA-ALCL cases were mainly associated with Silimed implants. Cases for other manufacturers were much lower.”</p>
26	Brotherston Chris, GC Aesthetics, United Kingdom	2. CONCLUSIONS	<p>For the Attention of the SCHEER Committee</p> <p>Please find our response to Point 2</p>  <p>GC_Aesthetics_Scheer_Point_2_4_Dec_2021</p> <p>Point 2</p>	<p>SCHEER agrees that the overall risk is low, as BIA-ALCL is generally described as an uncommon disease. However, available information clearly indicates that, as far as identified, the majority of BIA-ALCL cases are associated with certain types of macro-textured implants.</p> <p>It should be noted that a history of textured breast</p>

		<p>In this conclusion a statement was made that there is “moderate” evidence for a “causal” relationship between textured breast implants and BIA-ALCL. Although there is substantial clinical literature confirming that breast implants are associated with an increased risk of ALCL, Fitzal et al (2019) discusses that despite there being many studies looking at BIA-ALCL and its causes, it is not possible to estimate the risk of BIA-ALCL as there is not enough available data. Sundfield et al (2019) also states that it is unclear what the underlying pathogenesis and mechanisms are for BIA-ALCL. Finally, Prantl et al (2020) supports this view point also stating: “The rarity of the disease along with insufficient data on women with breast implants and breast implant sales contributes to insufficient statistical information”. Breast implants are also not the only denominator in the development of ALCL in the breast (Sundfield et al, 2019). In 2019, Bergsten et al presented a rare case of primary cutaneous ALCL of the breast in a patient with no known history of breast implants discussing that, as with any cancer, ALCL can present without any known implant cause.</p> <p>Without any definite knowledge of the pathology or aetiology GC Aesthetics would therefore state that until the pathogenesis of BIA-ALCL is known, they would contend the overall risk as low and a causal relationship, albeit moderate cannot be substantiated.</p> <p>References  Bergsten TM, 1, Principe DR, Raicu A, Rubin J, Ong AL, Hagen C. Non-implant associated primary cutaneous anaplastic large cell lymphoma of the breast <i>Journal of Surgical Case Reports</i>, 2019;5, 1–3  Fitzal F, Turner SD, Kenner L. Is breast implant-associated anaplastic large cell lymphoma a hazard of breast implant surgery? <i>Open Biol</i> 2019 9:190006  Prantl L, Gerken M, Zeman F, Leitzmann M, Koller M, Klinkhammer-Schalke M, Evert M, Kuehlmann B, Biermann N. Incidence of Anaplastic Large Cell Lymphoma and Breast-Implant-Associated Lymphoma—An Analysis of a Certified Tumor Registry over 17 Years. <i>J. Clin. Med.</i> 2020, 9, 1247; doi:10.3390/jcm9051247  Sundfeld D, Real S, Resendes B. Breast implant-associated anaplastic large-cell lymphoma: a systematic literature review. <i>Rev. Bras. Cir. Plást.</i></p>	<p>implants/expanders appears to be necessary but not sufficient for the development of BIA-ALCL.</p> <p>Doren et al., U.S. Epidemiology of Breast Implant-Associated Anaplastic Large Cell Lymphoma. <i>Plast Reconstr Surg.</i> 2017 May;139(5):1042-1050.</p> <p>Text was added in 4.4.1. on ALCL.</p> <p>“In a recent survey of a tumor registry only 12 ALK- and CD30+ ALCL cases were observed non of which was located in the breast tissue (Prantl et al., 2020).”</p> <p>References Fitzal et al. 2019 and Prantl et al. are now included.</p> <p>Fitzal F, Turner SD, Kenner L. Is breast implant-associated anaplastic large cell lymphoma a hazard of breast implant surgery? <i>Open Biol</i> 2019 9:190006</p> <p>Prantl L, Gerken M, Zeman F, Leitzmann M, Koller M, Klinkhammer-Schalke M, Evert M, Kuehlmann B, Biermann N. Incidence of Anaplastic Large Cell Lymphoma and Breast-Implant-Associated Lymphoma—An Analysis of a Certified Tumor Registry over 17 Years. <i>J. Clin. Med.</i> 2020, 9, 1247; doi:10.3390/jcm9051247</p>
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27	Mercer Nigel, Plastic, Reconstructive and Aesthetic Expert Advisory Group (PRASEAG), United Kingdom	2. CONCLUSIONS	<p>P8 Line 29: We are advised not to use the term ‘rare’ in the United Kingdom when referring to occurrence because it means ‘vanishingly rare’ in legal terms. Patients tend to assume ‘rare’ means that it will not happen to them.</p> <p>P9 line 1-2: ‘Based on the moderate weight of evidence, the SCHEER concludes there is a causal relationship between textured breast implants and BIA-ALCL.’ Until the cause and pathogenesis are proven, texture should, scientifically, remain ‘an association’.</p> <p>The document also ignores the literature on the benefits of texturing, especially relating to capsule formation when implants are inserted in the sub-mammary position.</p> <p>P9 Line 2-5: Suggestion fat transfer and flaps are an alternative in all cases is incorrect. Applicability depends patient wishes, on having sufficient fat or tissue for a autogenous flap and cost.</p>		<p>The Mandate of the Commission is an officially published EU document and as such cannot be modified.</p> <p>The term ‘rare’ was changed to ‘uncommon’ occurrence.</p> <p>SCHEER considers that as almost all implants, as far as identified in BIA-ALCL cases, were textured, this is a sufficient reason to use the term causal relationship. However, in the final Opinion, it is also now stated that in view of the uncommon occurrence of BIA-ALCL, it is clear that not all textured implants may result in BIA-ALCL. It should be noted that a history of textured breast implants/expanders appears to be necessary but not sufficient for the development of BIA-ALCL.</p> <p>SCHEER acknowledges that the availability of various types of breast implants is essential for optimal patient care.</p> <p>The alternatives have been addressed and text has been added.</p> <p>Modified text:</p> <p>However, patients’ characteristics may limit the application of these techniques.</p>
28	Hamdi Moustapha , European Master of surgical oncology, reconstructive	2. CONCLUSIONS	<p>My comments are on several points and levels.</p> <p>I outlined the text that I commented in red</p>		<p>SCHEER agrees with the comments raised, that a variety of breast implants are available to suit a range of patients with a variety of clinical and aesthetic needs. Furthermore, SCHEER is aware that the use of breast implants can be accompanied by complications. For example, regarding the use of the newer generation of smooth</p>


	<p>and aesthetic breast surgery</p> <p>Vrij Universiteit Brussel (VUB) – Belgium</p> <p>Universitat Autònoma de Barcelona, Spain</p> <p>, Belgium,</p>		 <p>Hamdi_scheers_comments.pdf</p>	<p>implants, there is some controversy in the literature regarding the number of complications that can occur compared to the use of textured implants and vice versa. Hence, SCHEER does not recommend removal of all textured implants from the market. However, based on the evaluated evidence, SCHEER has concluded that there is a clear association between the occurrence of BIA-ALCL and the presence of textured implants. This is the main subject of the Opinion and therefore, information regarding techniques used for breast augmentation surgery and types of implants available is provided purely as background information and therefore is not extensively discussed in the report.</p> <p>We agree that there is a need for an unambiguous, clinically validated classification system for breast implants including more parameters than just “surface roughness”.</p> <p>The importance of adequate registries is one of the recommendations of SCHEER.</p> <p>SCHEER as an independent advisory committee does not have a role to play in advising on standards of care</p>
29	<p>Decaluwé Kelly, Federal Agency of Medicines and Health Products, Belgium</p>	<p>2. CONCLUSIONS</p>	<p>Line 33-34  When considering the high number of cases lacking implant history details and the 1 pure smooth implant BIA-ALCL case reported in the USA, the FAMHP believes it to be more appropriate to write: 'The common factor underlying the occurrence of BIA-ALCL reported in all well-documented cases is the presence of textured implants.'</p>	<p>Text on causal relationship has been adapted.</p> <p>Text modified:</p> <p>“Based on these data SCHEER considers that there is a moderate weight of evidence for a causal relationship between textured breast implants and BIA-ALCL, particularly in relation to implants with an intermediate to high surface roughness.</p>

				<p>At this point it should be noted that i) there are several types of textured implants ii) surface textures of breast implants are not all manufactured in the same way, and iii) implants with diverse surface textures may also present different benefits. The magnitude of the risk per type of textured implant is difficult to establish due to the low incidence of the risk. Even with macro-textured implants, BIA-ALCL has a very low incidence. Therefore, risk assessments per implant type are needed. Furthermore, the risk should be weighed against the benefits. There is also a need for an unambiguous, clinically validated classification system for breast implants including more parameters than just “surface roughness”. A history of textured breast implants/expanders appears to be necessary but not sufficient for the development of BIA-ALCL.”</p>
30	CAMPANALE ANTONELLA, ITALIAN MINISTRY OF HEALTH, Italy	2. CONCLUSIONS	<p>P. 9 line 1-2: “Based on a moderate weight of evidence, the SCHEER concludes that there is a causal relationship between textured breast implants and BIA-ALCL” The IMoH would like to underline that most of the published studies on the BIA-ALCL are low evidence studies (IV to VII level of evidence), thus the above sentence must be considered wrong and we wonder what is the moderate scientific evidence that WG is talking about when they state that there is a “causal relationship” between textured breast implants and ALCL. Once more, we do believe that the WG should not be misunderstood the association found and showed in Literature with the causal relationship.</p>	<p>Text on causal relationship has been adapted.</p> <p>Text modified:</p> <p>“Based on these data, SCHEER considers that there is a moderate weight of evidence for a causal relationship between textured breast implants and BIA-ALCL, particularly in relation to implants with an intermediate to high surface roughness.</p> <p>At this point it should be noted that i) there are several types of textured implants ii) surface textures of breast implants are not all manufactured in the same way, and iii) implants with diverse surface textures may also present different benefits. The magnitude of the risk per type of textured implant is difficult to establish due to the low incidence of the risk. Even with macro-textured implants, BIA-ALCL has a very low incidence. Therefore, risk assessments per implant type are needed. Furthermore, the risk should be weighed against the benefits. There is also a need for an unambiguous, clinically validated classification system for breast implants including more parameters than just “surface roughness”. A history of textured breast implants/expanders appears to be necessary but not sufficient for the development of BIA-ALCL.”</p>

31	Salman Ahmed, Auralia, Ireland	2. CONCLUSIONS	<p>Dear SCHEER committee,</p> <p>I am a patient care provider with 17-year experience in breast augmentation surgery, with over 3,000 breast surgeries completed. I am not sponsored by any company. I have a vast experience in both textured implants and polyurethane. With textured devices, I have completed 800 procedures of which 385 were anatomical. With polyurethane coated implants, over 2300 patients. My primary goal is to help my patients achieving the desired aesthetic outcome with the minimal amount of surgery in order to reducing short and long-term complications. I constantly seek to maintain the integrity of breast tissue, leaving it possible to maintain a healthy breast tissue.</p> <p>To date I only use polyurethane coated implants, especially with an anatomical shape as a natural looking breast is more desirable for my patients. I mainly adopt the sub-mammary position.</p> <p>In the short term, anatomical polyurethane implants placed in sub-mammary position provide a soft breast with a very natural look and natural movement. The use of the polyurethane foam prevents rotation, cleavage, animation deformity, bottoming out, and rippling. More and more women are dedicated to fitness and exercise. If the only choice open to them would be round smooth implants, then there would be a significant increase in animation deformity when exercising because breast implants should be placed in sub-pectoral position in order to minimize any rotation. Moreover, a round implant placed in sub-mammary position to avoid breast animation will give a not natural look due to the fact that these women are usually very thin.</p> <p>In the long term, anatomical polyurethane implants placed in sub-mammary position allow to reduce the overall number of surgeries due to the incredibly low capsular contracture rate (less than 1% in my experience). Revision surgeries are also strongly reduced by the lack of long term bottoming out and rotation. Long lasting results are due to the integration of the fibrous capsule into the surrounding tissue, and to the stable form leading to less rippling. The use of polyurethane implants reduces the need for mastopexy with grade I/II ptosis because the re-draping of the breast tissue over an adherent implant helps the correction and, sometimes, avoids an unsightly mastopexy scar.</p> <p>Generally speaking, polyurethane implants are a cost-effective choice as less surgeries are needed to fix complications.</p>	<p>SCHEER agrees with the comments raised, that a variety of breast implants should be available to suit a range of patients with a variety of clinical and aesthetic needs. Furthermore, SCHEER is aware that the use of breast implants can be accompanied by complications. For example, regarding the use of the newer generation of smooth implants, there is some controversy in the literature regarding the number of complications that can occur compared to the use of textured implants and vice versa. Hence, SCHEER does not recommend removal of all textured implants from the market. However, based on the evaluated evidence, SCHEER has concluded that there is a clear association between the occurrence of BIA-ALCL and the presence of textured implants. This is the main subject of the opinion and therefore, information regarding techniques used for breast augmentation surgery and types of implants available is provided purely as background information and therefore is not extensively discussed in the report.</p>
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			<p>In your opinion, it would be advisable to withdraw even polyurethane implants from the market in order to reduce the eventuality of a very rare risk of BIA-ALCL. The purpose of my comment is to put you in front of the concrete complications that this decision would cause.</p> <p>There will be a large cohort of women who will suffer great mental anguish as they feel they have a ‘defected’ implant in their body. Those women will end up choosing to go for an unnecessary implants removal for the fear of BIA-ALCL.</p> <p>In conclusion, the strong reduction of the number of surgeries thanks to the use of polyurethane implants allows to reduce the surgery costs and the loss of income; less down time; less risk of surgery, comorbidity, and mortality; less destruction of the breast tissue from multiple surgeries; less psychological trauma for the patients.</p> <p>On the contrary, the suggested use of round smooth implants will increase significantly the number of surgeries due to the very high capsular contracture rate, bottoming out, the very high risk of implant flip/posterior rotation, parenchymal thinning, and ptosis.</p> <p>I strongly advise against making drastic decisions in favor of smooth implants in order to avoid the complications described above.</p>	
32	Geertsma Robert, RIVM - National Institute for Public Health and the Environment, Netherlands	2.1 Answers to the Terms of References	<p>2.1 – 4 ; p.10, lines 6-11 Surface roughness alone is not sufficient to classify a breast implant surface appropriately. The manufacturing method, as mentioned here, is also an important parameter. In addition, the surface area ratio should be included. This is recommended by an International WG of regulators, representatives of breast implant registries and academics. Their report is expected to be published soon. The reference will be submitted to SCHEER as soon as it is available. This report will be used as input into the revision process of ISO 14607, which is currently being initiated.</p> <p>2.1 – 5 ; p.10, lines 22-24 Statements on a moderate level of evidence for a causal relationship between textured breast implants and ALCL imply that a causal relationship exists between ALCL and all types of textured implants. As can be concluded from multiple statements in the body of the Opinion, stratification between the relative risks of various types of textures</p>	<p>2.1 – 4 ; p.10, lines 6-11 and 2.1 – 5 ; p.10, lines 22-24: Text on causal relationship and surface characterization is adapted:</p> <p>Text modified:</p> <p>“Based on these data, SCHEER considers that there is a moderate weight of evidence for a causal relationship between textured breast implants and BIA-ALCL, particularly in relation to implants with an intermediate to high surface roughness.</p> <p>At this point it should be noted that i) there are several types of textured implants ii) surface textures of breast implants are not all manufactured in the same way, and iii) implants with diverse surface textures may also present different benefits. The magnitude of the</p>

		<p>(including no texture) is currently not possible. In order to provide an honest and complete picture of current knowledge, this should be explained carefully in the Opinion, and certainly also in the answer to the specific question on this in the conclusion section, which is likely to undergo a much broader dissemination than the entire report. Furthermore, it is important also to point out that implants with different surface textures may also have different benefits, so in order to draw conclusions, a full benefit-risk evaluation should be made.</p> <p>2.1 – 5 ; p.10, lines 35-37  Agreed – previous implant history is crucial. Unfortunately is it often unknown. This does not only have impact on decisions for explantation, but also generally on conclusions with regard to the causal relationship between textured breast implants and ALCL. This should be taken into account more clearly in the Opinion.</p> <p>2.1 – 5 ; p.10, lines 46-47  “reported high-risk ISO macrotextured classification breast implants (e.g. polyurethane, salt-loss macrotextured, etc” is an imprecise statement, see also previous comments; it should be deleted. The example of manufacturer recalled devices is sufficient and not imprecise.</p> <p>2.1 – 6 ; p.11, lines 5-6  As can be concluded from multiple statements in the body of the Opinion, stratification between the relative risks of various types of textures (including no texture) is currently not possible. In order to provide an honest and complete picture of current knowledge, this should be explained carefully in the Opinion, and certainly also in the answer to a specific question on this in the conclusion section, which is likely to undergo a much broader dissemination than the entire report.</p> <p>2.1 – 6 ; p.11, lines 11-13  In order to state that this is an appropriate control measure, a full benefit-risk evaluation needs to be done – the control measure is only appropriate if benefit risk ratio changes in a positive way.</p>	<p>risk per type of textured implant is difficult to establish due to the low incidence of the risk. Even with macro-textured implants, BIA-ALCL has a very low incidence. Therefore, risk assessments per implant type are needed. Furthermore, the risk should be weighed against the benefits. There is also a need for an unambiguous, clinically validated classification system for breast implants including more parameters than just “surface roughness”. A history of textured breast implants/expanders appears to be necessary but not sufficient for the development of BIA-ALCL.”</p> <p>2.1 – 5 ; p.10, lines 35-37.</p> <p>As far as known, a textured implant was present or was noted in the patient’s history in all but one of the cases where the history was known (with one exception).</p> <p>2.1 – 5 ; p.10, lines 46-47. See above. As far as known, in all but one of the cases where the history is known, a textured implant (salt-loss macro-textured) or PU coated with a high surface roughness was present or was noted in the history of the patient. The reference to the ISO classification statement has been deleted.</p> <p>2.1 – 6 ; p.11, lines 5-6</p> <p>Text added:</p> <p>“However, it is not yet possible to determine the relative risk for BIA-ALCL of various surface characteristics. Therefore, there is a need for an unambiguous, clinically validated classification system for breast implants including more parameters than just “surface roughness”.”</p> <p>2.1 – 6 ; p.11, lines 11-13</p>
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			<p>2.1 – 8 ; p.11, lines 41-47</p> <p>The first two lines contain a very important statement - it belongs in the executive summary. It also shows why general statements about causal relationship between texture and BIA-ALCL cannot be made. In the rest of this paragraph, however, firstly surface roughness should not be singled out as the classification parameters, and secondly, two things are mixed here: the need for a universal grading system and further research into relation of surface characteristics with other parameters.</p>	<p>SCHIEER agrees, but based on the current knowledge on the causal relationship between BIA-ALCL and textured surface implants,,there is a very low incidence of BIA-ALCL, even in the presence of macro-textured implants.</p> <p>In addition, as most of the BIA-ALCL cases were observed for two specific types of implants (Biocell and Silimed), it cannot be excluded that the manufacturing process of these two implant types might be responsible. This would mean that with the removal of these two types of implants form the market, the number of cases should decrease for future breast implant procedures.</p> <p>Based on epidemiology, the text of the conclusion in section 6 was expanded by the addition of this sentence:</p> <p>“As far as the manufacturer for textured implants was known, most cases were found for the Biocell implant (texture manufactured by the salt loss technique), while for PU coated breast implants, BIA-ALCL cases were mainly associated with Silimed implants. Cases for other manufacturers were much lower.”2.1 – 8 ; p.11, lines 41-47</p> <p>Text has been adapted:</p> <p>“Research should be conducted to identify surface characteristics, which contribute to BIA-ALCL development. This should include research on the role of surface characteristics in relation to particle shedding and surface characterisation related to chemical moieties for their carcinogenic potential.”</p>
33	Govreen-Segal Dael	2.1 Answers to the Terms of References	<p>From page 9 row 11 to page 11 row 13</p> <p> Response_to_SCHEE R_preliminary_opinio</p>	<p>Comment Q 1. Text adapted.</p> <p>The clinical indications for the use of a specific type of breast implant should depend on a consultation between clinician and patient to allow informed decision making to take place with regards to the choice of an appropriate breast implant. For breast reconstruction a shared consultation with a multidisciplinary healthcare team including a pathologist, oncologist, surgeon, breast care nurse, etc., should be</p>

			<p>held with the patient to allow informed decision making to take place with regards to the breast reconstruction procedure as well as the choice of implant. For both aesthetic and reconstructive surgery all aspects of breast implants should be evaluated and discussed with the patient, expressly covering advantages, disadvantages, follow-up procedures and risk factors.</p> <p>Comment Q 2. Comment on spontaneous regression.</p> <p>Text in 4.5 modified.</p> <p>“Based on the epidemiology, it was suggested that the uncommon occurrence of BIA-ALCL might be a consequence of spontaneous regression/resolution of the disease (Fleming et al., 2018, 2020, 2020). To date, true cases of spontaneous regression/resolution of BIA-ALCL have not been reported. Of note, cases described by Fleming as spontaneously regressing were treated, and only reduced numbers of BIA-ALCL cell numbers were observed rather than a complete absence. In general BIA_ALCL has a favourable prognosis.....”</p> <p>Fleming D, Stone J, Tansley P. Spontaneous Regression and Resolution of Breast Implant-Associated Anaplastic Large Cell Lymphoma: Implications for Research, Diagnosis and Clinical Management. <i>Aesthetic Plast Surg.</i> 2018 Jun;42(3):672-678. doi: 10.1007/s00266-017-1064-z. Epub 2018 Feb 14.</p> <p>Fleming D, Stone J, Tansley P. Spontaneous Regression and Resolution of Breast Implant-Associated Anaplastic Large Cell Lymphoma: Implications for Research, Diagnosis and Clinical Management. <i>Aesthetic Plast Surg.</i> 2020 Aug;44(4):1109-1115. doi: 10.1007/s00266-020-01810-2. Epub 2020 Aug 5.</p> <p>Fleming D, Stone J, Tansley P. Update: Spontaneous Regression and Resolution of Breast Implant-Associated Anaplastic Large Cell Lymphoma—Implications for Research, Diagnosis and Clinical Management—Our Reflections and Current Thoughts Two Years On. <i>Aesth Plast Surg</i> (2020) 44:1116–1119</p>
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			<p>Comment Q3. Text adapted.</p> <p>“The estimation of the lifetime incidence of BIA-ALCL in women with implants has increased as presented in initial reports from 1 per million to current highest estimates of approximately 1 per 3000 women in Australia and the Netherlands.”</p> <p>Comment Q4.</p> <p>The current practice for surface characterization is indicated. SCHEER is aware that many other different properties of breast implants are part of the characterization process. SCHEER also recommends continuing work to determine the role of various surface characteristics in relation to the clinical appearance of BIA-ALCL.</p> <p>Comment Q5.</p> <p>As far as known almost all (probably except one) cases of which the history is known a textured implant was present or has been noted in the history of the patient. So, based on the current knowledge the causal relationship between BIA-ALCL and a textured surface is demonstrated, even when, also with the presence of a macro-textured implants, BIA-ALCL does have a very low incidence. Text on causal relationship with textured implants is adapted.</p> <p>“Based on these data, SCHEER considers that there is a moderate weight of evidence for a causal relationship between textured breast implants and BIA-ALCL, particularly in relation to implants with an intermediate to high surface roughness.</p> <p>At this point it should be noted that i) there are several types of textured implants ii) surface textures of breast implants are not all manufactured in the same way, and iii) implants with diverse surface textures may also present different benefits. The magnitude of the risk per type of textured implant is difficult to establish due to the low incidence of the risk. Even with macro-textured implants, BIA-ALCL has a very low incidence. Therefore, risk assessments per implant type</p>
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				<p>are needed. Furthermore, the risk should be weighed against the benefits. There is also a need for an unambiguous, clinically validated classification system for breast implants including more parameters than just “surface roughness”. A history of textured breast implants/expanders appears to be necessary but not sufficient for the development of BIA-ALCL.”</p> <p>Comment Q6.</p> <p>SCHEER also identifies the presence of a textured implant as a risk factor, but also identifies factors related to the possible aetiology of BIA-ALCL.</p> <p>The text has been adapted:</p> <p>“The factor that determines the risk of BIA-ALCL is the presence of an implant with a textured or rough surface, i.e. not smooth surface. In addition, a certain type of PU implant manufacturing process might also result in a risk for BIA-ALCL. However, it is not yet possible to determine the relative risk for BIA-ALCL of various surface characteristics. Therefore, there is a need for an unambiguous, clinically validated classification system for breast implants including more parameters than just “surface roughness”. A history of textured breast implants/expanders appears to be necessary but is not sufficient for the development of BIA-ALCL.”</p>
34	De Mezerville Roberto, Establishment Labs, Costa Rica	2.1 Answers to the Terms of References	<p>COMMENT: It is stated that “The clinical indications for the use of a specific type of breast implant do not depend on the preoperative clinical conditions, but only on the clinician’s and patient’s preferences, and consequently on industry and/or media information.”</p> <p>RECOMMENDATION: Given the extensive and broad studies and research that provides input into the utility and impact of the different options, we suggest that the committee acknowledges that there is</p>	<p>SCHEER agrees with this comment in that the choice of breast implant should not be driven by commercial aspects, but rather by the most appropriate implant for that specific patient with selection based on the most up-to-date scientific evidence available.</p> <p>Text adapted:</p>

			<p>sufficient evidence-based medicine to support that pre-operative clinical conditions are considered in the selection of the type of breast implant and that it does not only depend on external influences.</p>	<p>“The clinical indications for the use of a specific type of breast implant should depend on a consultation between clinician and patient to allow informed decision making to take place with regards to the choice of an appropriate breast implant. For breast reconstruction a shared consultation with a multidisciplinary healthcare team including a pathologist, oncologist, surgeon, breast care nurse, etc. should be held with the patient to allow informed decision making to take place with regards to the breast reconstruction procedure as well as the choice of implant. For both aesthetic and reconstructive surgery all aspects of breast implants should be evaluated and discussed with the patient, expressly covering advantages, disadvantages, follow-up procedures and risk factors.</p>
35	De Mezerville Roberto, Establishment Labs, Costa Rica	2.1 Answers to the Terms of References	<p>SECTION 8 Further research should be defined to provide continuation on the significant body of scientific information currently published, since the advice from SCHEER in October 2017 related to BIA-ALCL. A robust patient focused risk assessment should be developed not only to address the current possible variables identified until now but to cover every potential risk factor and the etiology of BIA-ALCL.</p> <p>As a member of the ISO Technical Committee under WG6 for the International Organization for Standardization (ISO) that actively participated on the last revision of the ISO 14607:2018, “Non-active surgical implants – Mammary implants – Particular requirements” it is of great value to the industry to continue the work done by the committee and by all the breast implant manufacturers updating the surface characterization under “Annex H; Tests for Surface Characteristics”. As stated in the standard in section H.6 “Expression of results: The obtained data is meant to generate information to improve knowledge on the correlation of texture characteristics, performance and safety”.</p> <p>Precisely to follow up with the main purpose of the ISO standard by classifying the surface of the breast implants, the scientific and clinical publications should be addressed to relate the surface description to the performance and/or safety as the note on section H.6 “Note: The</p>	<p>It is not the task of SCHEER to recommend that the plastic surgery societies should focus their efforts in educating a generation of European surgeons on the best practices for transitioning from textured breast implants to smooth devices. In most if not all BIA-ALCL cases, the breast implants showed textured surfaces. Several comments addressed the issue that not all breast implants surfaces are macro-textured. Therefore, the text on textured surfaces was modified.</p> <p>“Based on these data, SCHEER considers that there is a moderate weight of evidence for a causal relationship between textured breast implants and BIA-ALCL, particularly in relation to implants with an intermediate to high surface roughness.</p> <p>At this point it should be noted that i) there are several types of textured implants ii) surface textures of breast implants are not all manufactured in the same way, and iii) implants with diverse surface textures may also present different benefits. The magnitude of the risk per type of textured implant is difficult to establish due to the low incidence of the risk. Even with macro-textured implants, BIA-ALCL has a very low incidence. Therefore, risk assessments per implant type are needed. Furthermore, the risk should be weighed against the benefits. There is also a need for an unambiguous, clinically validated</p>

			<p>data resulting from the test at this point in time cannot be related to the performance or safety of the device, but enough data points should be collected to have the ability to study this relation”</p> <p>Furthermore, in addition to defining the drivers and/or activators for BIA ALCL, I find concerning that the information presented by several of the participants at the session on Nov 16th suggesting that some smooth surfaces significantly increase the reoperation rates in comparison to textured surfaces. There are developments in terms of more advanced smooth surfaces which lower the inflammatory response reducing complications such as capsular contracture and no associated reports to BIA-ALCL. The Post-Market Surveillance Report of implants with the SmoothSilk smooth surface from Establishment Labs demonstrates a significant reduction in capsular contracture rates and no reports of BIA-ALCL. These findings are further supported by independent data from the Swedish (see page 25 of the attachment) and Australian registries.</p> <p>RECOMMENDATION: We respectfully ask that the SCHEER committee recommend that the plastic surgery societies should focus their efforts in educating a generation of European surgeons on the best practices for transitioning from textured breast implants to smooth devices.</p>	<p>classification system for breast implants including more parameters than just “surface roughness”. A history of textured breast implants/expanders appears to be necessary but not sufficient for the development of BIA-ALCL.”</p>
36	De Mezerville Roberto , Establishment Labs, Costa Rica	2.1 Answers to the Terms of References	<p>SECTION 4 As a member of the Technical Committee under WG6 for the International Organization for Standardization (ISO) that actively worked on the last revision of the ISO 14607:2018, “Non-active surgical implants – Mammary implants – Particular requirements” I want to clarify that the main objective of the committee including the “Tests for Surface Characteristics” in the informative “Annex H”, was to define an objective way to classify breast implants surfaces. As stated in the standard in section H.6 “Expression of results: The obtained data is meant to generate information to improve knowledge on the correlation of texture characteristics, performance and safety”. In this same section there is an important note that clarifies the use of this classification; “Note: The data resulting from the test at this point in time cannot be related to the performance or safety of the device, but</p>	<p>SCHEER agrees that the current surface characterization of breast implants is limited, and that a statement on textured surfaces is not right in relation to BIA-ALCL. The text on textured surfaces was adapted as follows:</p> <p>“Based on these data SCHEER considers that there is a moderate weight of evidence for a causal relationship between textured breast implants and BIA-ALCL, particularly in relation to implants with an intermediate to high surface roughness.</p>

		<p>enough data points should be collected to have the ability to study this relation”.</p> <p>Important to highlight that before this ISO revision, breast implants surfaces were randomly referred as Smooth, Microtextured and Macrotextured, terms widely used by manufactures, clinicians and even patients to refer to types of breast implants.</p> <p>Given the emerging risks associated with the breast implants’ surface attributes and possible relation with the safety and efficiency of the breast implants, a test method to characterize surfaces objectively was needed.</p> <p>The technical committee, which included health authorities and industry, considered that the most objective way to define the surface classification was to use current international standards focused on surface texture area included as reference in Annex H, such as the ISO 4287 “Geometrical product specification (GPS) – Surface Texture: Profile Method – Terms, definitions and surface texture parameters” developed by the “Technical Committee ISO/TC 57, Metrology and properties of surfaces” and the ISO 25178 “Geometrical product specifications (GPS) – Surface Texture: Areal” developed by the Technical Committee ISO/TC 213, Dimensional and geometrical product specifications and verification, in collaboration with the European Committee for Standardization (CEN) Technical Committee CEN/TC 290, Dimensional and geometrical product specification and verification, in accordance with the Agreement on technical cooperation between ISO and CEN.</p> <p>After reviewing all the information in this opinion on the safety of breast implants in relation to the BIA-ALCL stated by the SCHEER and the overwhelming body of evidence on the number of cases related to textured devices, it is clear that the objective of ISO 14607 related to surface classification is serving its purpose. Today, there is sufficient and objective reports from high vigilance countries, such as the US FDA, the Australian TGA, Health Canada and at the EU level, which evidence that surfaces classified as Microtextured and Macrotextured according to</p>	<p>At this point it should be noted that i) there are several types of textured implants ii) surface textures of breast implants are not all manufactured in the same way, and iii) implants with diverse surface textures may also present different benefits. The magnitude of the risk per type of textured implant is difficult to establish due to the low incidence of the risk. Even with macro-textured implants, BIA-ALCL has a very low incidence. Therefore, risk assessments per implant type are needed. Furthermore, the risk should be weighed against the benefits. There is also a need for an unambiguous, clinically validated classification system for breast implants including more parameters than just “surface roughness”.; A history of textured breast implants/expanders appears to be necessary but not sufficient for the development of BIA-ALCL.”</p> <p>SCHEER recognises the need for a more extensive characterization of breast implants, especially regarding their surfaces.</p> <p>Recommendation: “A universal grading system for implant surfaces and surface characterisation should be further explored. Research should be conducted to identify surface characteristics, which contribute to BIA-ALCL development. This should include research on the role of surface characteristics in relation to particle shedding and surface characterisation related to chemical moieties for their carcinogenic potential. Especially implants exposed to an <i>in vivo</i> environment (i.e. explants) should be evaluated for surface characteristics.”</p>
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			<p>ISO 14607:2018, Annex H are related to the safety of the device and represent a risk to the patients, having a much higher probability to develop BIA-ALCL.</p> <p>Every breast implant manufacture commercializing in the EU should comply with the requirements of the ISO 14607:2018 including updating the expression of results based on the average roughness measurements on the final device. With this information, the literature research performed by SCHEER, in addition to the scientific peer-reviewed publications attached to this comment, should be sufficient as stated by the SCHEER to establish a methodologically robust risk assessment, focused on patient risk-benefits, to define the association of BIA-ALCL development with implant surfaces; the decision to clearly state this relationship should not be postponed.</p>	
37	No agreement to disclose personal data	2.1 Answers to the Terms of References	<p>Page 9 Lines 42-52 ‘To indicate what is the state-of-the-art knowledge in terms of incidence of BIA-ALCL.’</p> <p>When describing the state-of-the-art knowledge in terms of incidence, and considering the interval from implantation to diagnosis, as identified in this preliminary opinion, could the opinion reflect the minimum mean length of follow-up that is reported by a data-set, before that data-set can be considered valid for the purposes of determining the true incidence of this condition?</p> <p>Does the data considered by SCHEER support an understanding that the perceived incidence of BIA-ALCL increases with length of follow-up available within a data set?</p>	<p>On Page 10, the latency time is indicated:</p> <p>“The disease latency varies between a few and up to 20 or more years”.</p> <p>Follow-up times are presented in the various chapters in which the studies are discussed, mainly in Chapter 6.1, 6.2, and 6.3.</p>
38	MELVIN Tom, HPRA, Ireland	2.1 Answers to the Terms of References	<p>Page 9 Lines 45-46 The incidence of BIA-ALCL is considered low, varies by implant type, and is associated with textured implants. Could SCHEER please describe the scale used to quantify the incidence as ‘low’, and please consider citing this in the report?</p> <p>When considering the relative risk with respect to the incidence of ALCL in the breast, BIA-ALCL is associated with a significantly raised incidence with an odds ratio of 421.8 (DeJong 2018).</p>	<p>SCHEER considers that because approximately 1100 cases of BIA-ALCL are currently known (Clemens MW, 2nd World Consensus Conference on BIA-ALCL, 6-7 November 2020, Houston, Tx, USA), and because millions of women have breast implants, the prevalence of BIA-ALCL can be considered as low.</p> <p>Reference is made to the paper of De Boer et al. 2018. De Boer M, van Leeuwen FE, Hauptmann M, Overbeek LIH, de Boer JP, Hijmering NJ, 52 Sernee A, Klazen CAH, Lobbes MBI, van der Hulst RRWJ, Rakhorst</p>

				<p>HA, de Jong D. Breast Implants and the Risk of Anaplastic Large-Cell Lymphoma in the Breast. JAMA 1 Oncol. 2018 Mar 1; 4(3):335-341.</p> <p>Even in this paper, 42 cases of ALCL were observed in 26 years of pathologic diagnosis, of which 32 out of 42 were associated with a breast implant.</p>
39	No agreement to disclose personal data	2.1 Answers to the Terms of References	Page 11, line 48-51 'The role of the aforementioned implant qualities in inducing chronic inflammation should be investigated including possible roles of particle shedding, bacterial contamination, and chemical moieties on the surface of breast implants' ANSM have completed testing on this topic – have SCHEER considered it for inclusion?	ANSM information was not available for the SCHEER.
40	No agreement to disclose personal data	2.1 Answers to the Terms of References	Page 11, line 42-43 '. Research should be conducted to identify surface roughness characteristics, which contribute to BIA-ALCL development.' TGA have done this in their report 'TGA Biomaterials and Engineering Laboratory Report: Non-active mammary implants' and consequent decisions. Have the implications of this report been considered by SCHEER?	<p>Page 11, line 42-43, describes considerations for improving surface characterization of breast implants. The TGA report has been considered but details were not included. Of specific relevance is the issue whether surface characteristics can be related to clinical outcomes. TGA report is now cited in section 4.6.</p> <p>"A recent TGA report has evaluated breast implants on the Australian market. (TGA 2019). The TGA concluded that the ISO method did not adequately describe the complexities of surface textures resulting from the myriad of texturing techniques manufacturers employ. Additionally, TGA employed micro-Computed Tomography to extend the categories for surface characterization and was able to group breast implants according to surface characteristics. These groupings include polyurethane-coated, closed salt-loss, open salt-loss, imprinting, subsurface gas diffusion, surface gas diffusion and smooth. It was concluded that the current classification systems require refinement and further examination to develop practical and clinical applications."</p> <p>Text was added in the conclusion of this section:</p> <p>"The ISO 14607:2018 is currently under revision as the classification based on surface roughness only was considered to limited as was</p>

				<p>also concluded in the TGA 2019 report.”</p> <p>TGA September 2019. Biomaterials &amp; Engineering Laboratory Report Project: Surface Topography Device: Non-active mammary implants. Therapeutic Goods Administration, Department of Health, Australian Government. Woden ACT 2606 Australia.</p>
41	No agreement to disclose personal data	2.1 Answers to the Terms of References	<p>Page 11, line 11-13 ‘Although the full aetiology is not yet understood, an appropriate control measure to reduce the identified risk is to limit the use of textured implants.’</p> <p>In response to specific ask number 6 of the Mandate, the committee has identified that an appropriate control measure to reduce the identified risk is to limit the use of textured implants. How would SCHEER advise that this control be applied?</p> <p>Does the SCHEER have an opinion as to how the extent of this control should be defined and whether the scientific evidence considered supports any degree of proportionality with respect to control measures based on relative risks of degrees of surface texturing?</p>	<p>SCHEER has modified the statement on textured implants:</p> <p>“Based on these data SCHEER considers that there is a moderate weight of evidence for a causal relationship between textured breast implants and BIA-ALCL, particularly in relation to implants with an intermediate to high surface roughness.</p> <p>At this point it should be noted that i) there are several types of textured implants ii) surface textures of breast implants are not all manufactured in the same way, and iii) implants with diverse surface textures may also present different benefits. The magnitude of the risk per type of textured implant is difficult to establish due to the low incidence of the risk. Even with macro-textured implants, BIA-ALCL has a very low incidence. Therefore, risk assessments per implant type are needed. Furthermore, the risk should be weighed against the benefits. There is also a need for an unambiguous, clinically validated classification system for breast implants including more parameters than just “surface roughness” A history of textured breast implants/expanders appears to be necessary but not sufficient for the development of BIA-ALCL.”</p> <p>How control measures (when needed) are implemented is not the remit of SCHEER. The refinement of the statement as presented here does allow for a more diverse use of textured implants with the</p>




				<p>exception of macro-textured implants.</p> <p>Text adapted:  “Although the full aetiology is not yet understood, an appropriate control measure to reduce the identified risk is to limit the use of macro-textured implants, notably those prepared by the salt loss technique, and those with a certain type of PU coating.”</p>
42	No agreement to disclose personal data	2.1 Answers to the Terms of References	<p>Page 11, line 10-11 notes ‘The most important criterion that is associated with the occurrence of BIA-ALCL is the type of surface characterising the implant.’</p> <p>Can any more detail be provided here on how this criterion is associated with the differences in the incidence of BIA-ALCL? For example, Page 30, lines 26-28 of this preliminary opinion notes that ‘implants that are ISO classified as macrotextured have been associated with a greater incidence of BIA-ALCL than microtextured’. See also Page 10 Lines 46-47 ‘reported high-risk ISO macrotextured classification breast implants (e.g. polyurethane, salt-loss macrotextured, etc.)’ More specific detail here would provide helpful context for the understanding of what the committee describes as an ‘appropriate control measure’ in the next sentence.</p>	<p>SCHEER has modified the statement on textured implants:</p> <p>“Based on these data, SCHEER considers that there is a moderate weight of evidence for a causal relationship between textured breast implants and BIA-ALCL, particularly in relation to implants with an intermediate to high surface roughness.</p> <p>At this point it should be noted that i) there are several types of textured implants ii) surface textures of breast implants are not all manufactured in the same way, and iii) implants with diverse surface textures may also present different benefits. The magnitude of the risk per type of textured implant is difficult to establish due to the low incidence of the risk. Even with macro-textured implants, BIA-ALCL has a very low incidence. Therefore, risk assessments per implant type are needed. Furthermore, the risk should be weighed against the benefits. There is also a need for an unambiguous, clinically validated classification system for breast implants including more parameters than just “surface roughness”. A history of textured breast implants/expanders appears to be necessary but not sufficient for the development of BIA-ALCL.”</p> <p>How control measures (when needed) are implemented is not the remit of SCHEER. The refinement of the statement as presented here does allow for a more diverse use of textured implants with the exception of macro-textured implants.</p> <p>Text adapted:</p>

				<p>“The full aetiology of BIA-ALCL is not yet understood, although an appropriate control measure to reduce the identified risk, is to limit the use of macro-textured implants, notably those prepared by the salt loss technique, and those with a certain type of PU coating.”</p>
43	No agreement to disclose personal data	2.1 Answers to the Terms of References	<p>Page 10, line 49-51 ‘In symptomatic patients with textured implants in place, implant removal with total capsulectomy is recommended.’ The HPRA would consider it necessary to provide further information regarding the meaning of ‘symptomatic’ in this context. In addition we think it would be important to explain why the recommendation is noted only for patients who need to have both symptoms and a textured implant? Please account for the occurrence of patients who do not know the type of implant surfacing for their implants at the time of symptoms.</p>	<p>SCHEER recommends only to remove an implant when there are symptoms that might indicate the presence of BIA-ALCL. Further investigation is in such cases necessary. This is described in more detail in Chapter 4.4.2. and 4.5. SCHEER does not recommend removal of all macro-textured implant as surgical procedures do have an inherent risk, and BIA-ALCL is an uncommon disease with a very low incidence. Also when the implant surface is not known implant removal is only recommended when there are symptoms indicating BIA-ALCL.</p> <p>Text adapted on page 10, line 41-44.</p> <p>“In non-symptomatic patients with textured implants or implants with unknown surface, implant removal with or without total capsulectomy for the single purpose of BIA-ALCL prophylaxis is not recommended due to the very low incidence of the disease.”</p>
44	No agreement to disclose personal data	2.1 Answers to the Terms of References	<p>Page 10, line 44-47 ‘However, some patients may request removal of the implant and capsule, particularly patients with manufacturer-recalled implants or the reported high-risk ISO macrot textured classification breast implants (e.g. polyurethane, salt-loss macrot textured, etc.).’ It is noted that some patients attribute a higher risk with certain types of implants, and requests for more invasive explantation with capsulectomy are being made.</p> <p>Can the SCHEER address this more thoroughly with reference to the scientific literature? Can the SCHEER please describe further what is meant by ‘reported high-risk ISO macrot textured classification breast implants’? Could the SCHEER provide more detail with respect to the relative risk of PU and macrot textured implants?</p>	<p>SCHEER identified a causal relationship between BIA-ALCL and textured breast implants mainly produced by the salt loss technique (Biocell) and a certain type of PU coating (Silimed). The relative risk cannot be determined as the denominator of the amount of women with a certain type of implant is not known. Breast implant registries that are currently initiated might give an answer to these questions in future evaluations.</p>
45	No agreement to	2.1	Page 10, line 44-47 ‘However, some patients may request removal of	SCHEER identified a causal relationship between BIA-ALCL and

	disclose personal data	Answers to the Terms of References	<p>the implant and capsule, particularly patients with manufacturer-recalled implants or the reported high-risk ISO macrotextured classification breast implants (e.g. polyurethane, salt-loss macrotextured, etc.).’ It is noted that some patients attribute a higher risk with certain types of implants, and requests for more invasive explantation with capsulectomy are being made.</p> <p>Can the SCHEER address this more thoroughly with reference to the scientific literature?  Can the SCHEER please describe further what is meant by ‘reported high-risk ISO macrotextured classification breast implants’?  Could the SCHEER provide more detail with respect to the relative risk of PU and macrotextured implants?</p>	<p>textured breast implants, mainly macro-textured produced by the salt loss technique (Biocell) and a certain type of PU coating (Silimed). The relative risk cannot be determined as the denominator of the amount of women with a certain type of implant is not known. Breast implant registries that are currently initiated might give an answer to these questions in future evaluations.</p>
46	No agreement to disclose personal data	2.1 Answers to the Terms of References	<p>Page 10, line 9-11 ‘The surface roughness can be described best by using the ISO classification 10 of roughness being: Smooth (50µm) based 11 on the implant average surface roughness (ISO 14607:2018).’ The ISO is not the best description available. The ISO is subject to revision as this aspect of the document is generally recognised as insufficient.</p> <p>ISO 14607: 2018, Annex H does not sufficiently take into account the complexities of surface textures which result from differences of texturing techniques which manufacturers use The TGA report - Biomaterials and Engineering Laboratory Report: Non-active mammary implants – does take the complexities into account and it should be cited and used in this report.</p>	<p>SCHEER agrees that also the ISO classification has its limits and is aware that the ISO 14607:2018 is currently under revision.</p> <p>TGA report is now cited in section 4.6.</p> <p>“A recent TGA report has evaluated breast implants on the Australian market. (TGA 2019). The TGA concluded that the ISO method did not adequately describe the complexities of surface textures resulting from the myriad of texturing techniques manufacturers employ. Additionally TGA employed micro-Computed Tomography to extend the categories for surface characterization and was able to group breast implants according to surface characteristics These groupings include polyurethane-coated, closed salt-loss, open salt-loss, imprinting, subsurface gas diffusion, surface gas diffusion and smooth. It was concluded that the current classification systems require refinement and further examination to develop practical and clinical applications.”</p> <p>Text was added in the conclusion of this section:</p> <p>“The ISO 14607:2018 is currently under revision as the classification based on surface roughness only was considered too limited as was also concluded in the TGA 2019 report.”</p>

				TGA September 2019. Biomaterials & Engineering Laboratory Report Project: Surface Topography Device: Non-active mammary implants. Therapeutic Goods Administration, Department of Health, Australian Government. Woden ACT 2606 Australia
47	No agreement to disclose personal data	2.1 Answers to the Terms of References	<p>Page 9, line 17-20 'The clinical indications for the use of a specific type of breast implant do not depend on the preoperative clinical conditions, but only on the clinician's and patient's preferences, and consequently on industry and/or media information.'</p> <p>HPRA would be grateful for clarification of this text. Does this mean that no patient has a clinical need for polyurethane foam coated, macrotextured or other implant texturing? If so, are these preferential type criteria sufficient to justify a potentially increased relative risk with more highly textured implants?</p>	<p>Health Products Regulatory Authority (HPRA) Formerly known as the Irish Medicines Board (IMB),</p> <p>SCHEER agrees with this comment in that the choice of breast implant should not be driven by commercial aspects, but rather by the most appropriate implant for that specific patient with selection based on the most up-to-date scientific evidence available.</p> <p>Text adapted:</p> <p>"Clinical indications for the use of a specific type of breast implant should depend on a consultation between clinician and patient to allow informed decision making to take place with regards to the choice of an appropriate breast implant. For breast reconstruction a shared consultation with a multidisciplinary healthcare team including a pathologist, oncologist, surgeon, breast care nurse, etc should be held with the patient to allow informed decision making to take place with regards to the breast reconstruction procedure as well as the choice of implant. For both aesthetic and reconstructive surgery all aspects of breast implants should be evaluated and discussed with the patient, expressly covering advantages, disadvantages, follow-up procedures and risk factors."</p>
48	Cerkes Nazim, ISAPS,	2.1 Answers to	6. To describe the factors that may determine the risk of BIA-ALCL. To identify criteria regarding the characterisation of breast implants in	Comment Q6.

	international	the Terms of References	<p>relation to ALCL and control measures to reduce the identified risk.</p>  <p>addendum_to_ISAPS_COMMENT_on_SCHI</p> <p>We believe that the exclusive association of BIA-ALCL with textured implants cannot be demonstrated with the existing data, also referring to the FDA Medical Device Reports, as of January 2020. There is a need for more high-quality, multivariate analyses with adequate power or systematic review of these studies to reach a more educated conclusion.</p> <p>7. In the context of ALCL to briefly describe alternatives to breast implants. In order to accommodate the individual clinical situation in each patient it is essential to emphasize the need for each surgeon of having a complete range of breast implants, both for breast augmentation and breast reconstruction. An eventual ban on textured implants will prevent the use of anatomical implants which will have an impact on the quality of outcomes. Besides this the unique use of smooth round implants could cause further issues, from a cost-effectiveness and risk-benefit point of view. More complication will necessitate more re-operations and this with less individualized results and less happy patients. The eventual ban of textured implants will prevent the use of anatomical implants which is the gold standard in some patients particularly in reconstructive cases. The suggestion that reconstruction with autologous tissues is the solution is not acceptable for all the surgeons and patients (no long-term evidence, high costs, long surgical sessions, more procedures, etc.) Many slim patients do not have enough tissue or fatty tissue to undergo a fat grafting procedure that often needs revision and replication.</p> <p>8. Where relevant to identify needs for further research and the best ways to collect the missing data regarding breast implants and ALCL.</p>	<p>SCHEER identified a causal relationship between BIA-ALCL and textured breast implants, mainly macro-textured produced by the salt loss technique (Biocell) and a certain type of PU coating (Silimed). The relative risk cannot be determined as the denominator of the amount of women with a certain type of implant is not known. Breast implant registries that are currently initiated might give an answer to these questions in future evaluations.</p> <p>Text on textured implants has been modified:</p> <p>“Based on these data SCHEER considers that there is a moderate weight of evidence for a causal relationship between textured breast implants and BIA-ALCL, particularly in relation to implants with an intermediate to high surface roughness.</p> <p>At this point it should be noted that i) there are several types of textured implants ii) surface textures of breast implants are not all manufactured in the same way, and iii) implants with diverse surface textures may also present different benefits. The magnitude of the risk per type of textured implant is difficult to establish due to the low incidence of the risk. Even with macro-textured implants, BIA-ALCL has a very low incidence. Therefore, risk assessments per implant type are needed. Furthermore, the risk should be weighed against the benefits. There is also a need for an unambiguous, clinically validated classification system for breast implants including more parameters than just “surface roughness”. A history of textured breast implants/expanders appears to be necessary but not sufficient for the development of BIA-ALCL.”</p> <p>Comment Q7. Text on textured implants has been modified.</p> <p>Comment Q8. SCHEER agrees with this statement.</p>
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			As already mentioned in point three, we see it as the task of the national societies to assist the government in the creation of national registers. In this context, international linking through a worldwide register should be implemented in accordance with data protection law and already taken into account in the design. We explicitly support and cooperate with the ICOBRA registry.	
49	Cerkes Nazim, ISAPS, International	2.1 Answers to the Terms of References	<p>Spear SL, Murphy DK; Allergan Silicone Breast Implant U.S. Core Clinical Study Group. Natrelle round silicone breast implants: Core Study results at 10 years. <i>Plast Reconstr Surg.</i> 2014 Jun;133(6):1354-61.</p> <p>Singh N, Picha GJ, Hardas B, Schumacher A, Murphy DK. Five-Year Safety Data for More than 55,000 Subjects following Breast Implantation: Comparison of Rare Adverse Event Rates with Silicone Implants versus National Norms and Saline Implants. <i>Plast Reconstr Surg.</i> 2017 Oct;140(4):666-679.</p> <p>Maxwell GP, Van Natta BW, Bengtson BP, Murphy DK. Ten-year results from the Natrelle 410 anatomical form-stable silicone breast implant core study. <i>Aesthet Surg J.</i> 2015 Feb;35(2):145-55.</p> <p>Adams WP Jr, Culbertson EJ, Deva AK, R Magnusson M, Layt C, Jewell ML, Mallucci P, Hedén P. Macrot textured Breast Implants with Defined Steps to Minimize Bacterial Contamination around the Device: Experience in 42,000 Implants. <i>Plast Reconstr Surg.</i> 2017 Sep;140(3):427-431.</p> <p>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?). Regarding the classifications, we agree with SCHEER's assessment that the currently most useful classification is the ISO classification. We consider it necessary to put the definitions, which are mostly company-specific, on neutral ground by means of a revised classification. Here SCHEER could make its infrastructure available.</p> <p>5. To indicate whether a causal relationship between breast implants</p>	<p>SCHEER thanks Dr Cerkes for providing the literature references. However, as these references were not specifically dealing with BIA-ALCL cases, they were not further considered.</p> <p>The issue of bacterial contamination as possible source for a chronic inflammation, as also indicated in Adams et al. 2017, and subsequent lymphoproliferation has been addressed in section 6.4.</p> <p>Regarding comment 4. SCHEER is an independent advisory body of the EC, and as such does not have an infrastructure to commit itself to participation in ISO Technical Committees. SCHEER provides advice based on specific mandates published by the EC in which dedicated questions are raised. The text on characterisation of breast implant surfaces as described in ISO 14607:2018 has been modified.</p> <p>SCHEER agrees that also the ISO classification has its limits and is aware that the ISO 14607:2018 is currently under revision.</p> <p>Text adapted:</p> <p>“It should be noted that the ISO 14607:2018 is currently under revision as the classification based on surface roughness only was</p>

		<p>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. Due to the very diverse data and information available, it does not seem possible for us, as a scientific society, to establish a single causality with sufficient evidence. However, many studies suggest that chronic infections play a role.</p> <p>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. We believe that the exclusive association of BIA-ALCL with textured implants cannot be demonstrated with the existing data, also referring to the FDA Medical Device Reports, as of January 2020. There is a need for more high-quality, multivariate analyses with adequate power or systematic review of these studies to reach a more educated conclusion.</p>	<p>considered too limited as was also concluded in the TGA 2019 report.”</p> <p>TGA report is now cited in section 4.6.</p> <p>“A recent TGA report has evaluated breast implants on the Australian market. (TGA 2019). The TGA concluded that the ISO method did not adequately describe the complexities of surface textures resulting from the myriad of texturing techniques manufacturers employ. Additionally TGA employed micro-Computed Tomography to extend the categories for surface characterization and was able to group breast implants according to surface characteristics. These groupings include polyurethane-coated, closed salt-loss, open salt-loss, imprinting, subsurface gas diffusion, surface gas diffusion and smooth. It was concluded that the current classification systems require refinement and further examination to develop practical and clinical applications.”</p> <p>Text was added in the conclusion of this section:</p> <p>“The ISO 14607:2018 is currently under revision as the classification based on surface roughness only was considered too limited as was also concluded in the TGA 2019 report.”</p> <p>TGA September 2019. Biomaterials &amp; Engineering Laboratory Report</p> <p>Project: Surface Topography Device: Non-active mammary implants. Therapeutic Goods Administration, Department of Health, Australian Government. Woden ACT 2606 Australia</p> <p>Answer Q4 text added.</p>
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				benefits. There is also a need for an unambiguous, clinically validated classification system for breast implants including more parameters than just “surface roughness”. A history of textured breast implants/expanders appears to be necessary but not sufficient for the development of BIA-ALCL.”
50	Cerkes Nazim, ISAPS, International	2.1 Answers to the Terms of References	<p>1. To briefly describe the specific clinical indications and uses for various types of breast implants.</p> <p>We must firmly object to the assertion that the "... clinical indications for the use of a certain type of breast implant are not depend on the preoperative clinical conditions, but only on the preferences of patients and consequently to information from industry and/or the media".</p> <p>No literature references are given for this claim. It contradicts the daily clinical routine in aesthetic surgery. Many congresses and lectures are specifically dedicated to this topic where conflicts of interest must be regularly identified.</p> <p>2. To briefly describe what BIA-ALCL is, the specific diagnostic criteria, the state of the art treatment, and the prognosis of the disease. In relation to ALCL, the good clinical practices for the follow-up of women with breast implants should also be described.</p> <p>We fully agree with the statement on diagnostic criteria and treatment options as well as prognosis.</p> <p>It is particularly important to educate patients and all physicians about the importance of early diagnosis and the excellent prognosis of early treatment. This low mortality with millions of applications worldwide must be a further criterion in the final opinion of SCHEER.</p> <p>If a band on textured implants were to be issued now, it is to be expected that many patients would have their implants changed due to uncertainty, which would result in a not low morbidity with a mortality that should not be underestimated. This is likely to be significantly higher than the mortality caused by BIA-ALCL (unconfirmed</p>	<p>SCHEER agrees with this comment in that the choice of breast implant should not be driven by commercial aspects, but rather by the most appropriate implant for that specific patient with selection based on the most up-to-date scientific evidence available</p> <p>Text adapted:</p> <p>“Clinical indications for the use of a specific type of breast implant should depend on a consultation between clinician and patient to allow informed decision making to take place with regards to the choice of an appropriate breast implant. For breast reconstruction a shared consultation with a multidisciplinary healthcare team including a pathologist, oncologist, surgeon, breast care nurse, etc should be held with the patient to allow informed decision making to take place with regards to the breast reconstruction procedure as well as the choice of implant. For both aesthetic and reconstructive surgery all aspects of breast implants should be evaluated and discussed with the patient, expressly covering advantages, disadvantages, follow-up procedures and risk factors.</p> <p>2. It is not the task of SCHEER to recommend that the plastic surgery societies should focus their efforts in educating a generation of European surgeons on the best practices for transitioning from textured breast implants to smooth devices. In most if not all BIA-ALCL cases the breast implants showed textured surfaces. Several comments addressed the issue that not all breast implants surfaces are macro-textured. Therefore, the text on textured surfaces was modified.</p> <p>SCHEER has considered the evidence and concluded that there is a</p>

		<p>assumption).</p> <p>It is the opinion and practice of ISAPS to focus on both patient and surgeon education and to provide comprehensive information about the disease to patients and, family doctors. For example, we have cooperated with the international family doctor organization WONCA and organized large-scale webinars in which we informed the more than 500,000 general practitioners (often first contact with patients) worldwide about the serious first symptoms of BIA-ALCL and the next steps to be taken.</p> <p>In our opinion, the goal must be to provide more extensive education and training in order to treat the rare cases of BIA-ALCL at an early stage. We know from past breast implant scandals the unsubstantiated side effects in patients who are unsure about separating themselves from their implants with capsulectomy and thereby subjecting themselves to a not inconsiderable surgical risk.</p> <p>3. To indicate what knowledge is in terms of incidence of BIA-ALCL. It is not possible to determine the incidence of BIA ALCL due to the lack of a worldwide reporting system, also because the dominator is missing. We also underline our proposal to ensure that mandatory registry entries are introduced at the national level. Initial efforts to establish international registers are difficult for reasons known to us, such as data protection.</p> <p>Some additional literature may be also considered:</p> <p>Campanale A, Boldrini R, Marletta M. 22 Cases of Breast Implant-Associated ALCL: Awareness and Outcome Tracking from the Italian Ministry of Health.</p> <p>Coroneos CJ, Selber JC, Offodile AC 2nd, Butler CE, Clemens MW. US FDA Breast Implant Postapproval Studies: Long-term Outcomes in 99,993 Patients. <i>Ann Surg.</i> 2019 Jan;269(1):30-36. doi: 10.1097/SLA.0000000000002990.</p>	<p>moderate weight of evidence for a causal relationship between BIA-ALCL and textured breast implants. SCHEER has also identified the fact that the mechanism on the induction of BIA-ALCL by breast implants is not yet known, but considers local persistent inflammation as an important contributor.</p> <p>Text has been adapted on the textured implants.</p> <p>“Based on these data SCHEER considers that there is a moderate weight of evidence for a causal relationship between textured breast implants and BIA-ALCL, particularly in relation to implants with an intermediate to high surface roughness.</p> <p>At this point it should be noted that i) there are several types of textured implants ii) surface textures of breast implants are not all manufactured in the same way, and iii) implants with diverse surface textures may also present different benefits. The magnitude of the risk per type of textured implant is difficult to establish due to the low incidence of the risk. Even with macro-textured implants, BIA-ALCL has a very low incidence. Therefore, risk assessments per implant type are needed. Furthermore, the risk should be weighed against the benefits. There is also a need for an unambiguous, clinically validated classification system for breast implants including more parameters than just “surface roughness”.; A history of textured breast implants/expanders appears to be necessary but not sufficient for the development of BIA-ALCL”</p> <p>3. The Registries are mentioned in the recommendations of SCHEER.</p> <p>Literature specifically dealing with BIA-ALCL has been included.</p> <p>Campanala et al 2018, new citation included. Nava et al. 2017, new citation included.</p>
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51	Parreira Carlos, EASAPS ESAPS, Belgium	2.1 Answers to the Terms of References	<p>2.1.6. To describe the factors that may determine the risk of BIA-ALCL. To identify criteria regarding the characterization of breast implants in relation to ALCL and control measures to reduce the identified risk.</p> <p>Line 5: “The factor that determines the risk of BIA-ALCL is the presence of a textured, i.e. not smooth, breast implant.”</p> <p>Again, as mentioned before the overall majority of ALCL cases is related to Biocell, focusing this on all textured implants is not correct. A more appropriate wording would be the presence of a breast implant. More correct: “The factor that determines the risk of BIA-ALCL is the presence of breast implant.”</p> <p>SCHEER concluded in line 12 that “Although the full aetiology is not yet understood, an appropriate control to reduce the identified risk is to limit the use of textured implants”.</p> <p>Unfortunately, the committee does not advise on the negative consequences of removing all textured implants from the market, such as risk for capsular contracture in sub-glandular position, animation deformity, distortion, double contour deformities, malposition, increased need of mesh, unfavorable results in conditions such as congenital deformities of the breast or after massive weight loss and especially breast reconstruction, to mention some examples. A restriction to smooth implants only sets the patient at a today not objectively evaluated risk for revision surgery. As well as this, all revision surgery has the inherent risk of complications, which is higher when</p>	<p>SCHEER has considered the evidence and concluded that there is a moderate weight of evidence for a causal relationship between BIA-ALCL and textured breast implants. SCHEER has also identified the fact that the mechanism on the induction of BIA-ALCL by breast implants is not yet known, but considers local persistent inflammation as an important contributor.</p> <p>Text has been adapted on the textured implants.</p> <p>“Based on these data SCHEER considers that there is a moderate weight of evidence for a causal relationship between textured breast implants and BIA-ALCL, particularly in relation to implants with an intermediate to high surface roughness.</p> <p>At this point it should be noted that i) there are several types of textured implants ii) surface textures of breast implants are not all manufactured in the same way, and iii) implants with diverse surface textures may also present different benefits. The magnitude of the risk per type of textured implant is difficult to establish due to the low incidence of the risk. Even with macro-textured implants, BIA-ALCL has a very low incidence. Therefore, risk assessments per implant type are needed. Furthermore, the risk should be weighed against the benefits. There is also a need for an unambiguous, clinically validated classification system for breast implants including more parameters than just “surface roughness”. A history of textured breast implants/expanders appears to be necessary but not sufficient for the development of BIA-ALCL.”</p>

		<p>capsulectomy is done. The outcome of such a report could lead to unnecessary worry in patients who are perfectly happy with their results demanding revision surgery. This, while there is no evidence based apparent advantage of such a procedure compared to mere observation, is likely to produce some unhappy patients after revision surgery.</p> <p>The SCHEER statement on the insufficient actual classification of shell texture is unanimously agreed upon in our community. E(A)SAPS would like to forward the opinion that a reliable definition of texture should include the following factors: shell shedding particles, friction and adhesivity factors besides the roughness of the shell. This statement on insufficient actual classification also contradicts the statement “to limit the use of textured implants” , after Allergan removed their macro-textured implant from the market which was associated with the majority of ALCL cases there are no data indicating that all different types of texturization from Micro-textured on one end to Poly-urethane on the other hand pose the same association. Before making such a conclusion a universally agreed classification of texturization should be used and additional data obtained.</p> <p>Please change wording to:  “Although the full aetiology is not yet understood, an appropriate approach is to evaluate the fate of all breast implants in vivo. Mandatory registration of all breast implants should be promoted.”</p> <p>2.1.7. In the context of ALCL to briefly describe alternatives to breast implants.  “There are several alternatives to breast implants that involve plastic surgery techniques, either using autologous flap tissue or autologous fat transfer. However, these techniques are rarely used outside of reconstructive surgery. “</p> <p>This is a bit limited. please correct to:  “For aesthetic patients the alternatives are limited to autologous fat transfer. Unfortunately, this technique is only applicable in limited cases with low predictability. There are other alternatives to breast implants</p>	<p>The text on controlled measures has been modified.</p> <p>“The factor that determines the risk of BIA-ALCL is the presence of an implant with a textured or rough surface, i.e. not smooth surface. In addition, a certain type of PU implant manufacturing process might also result in a risk for BIA-ALCL. However, it is not yet possible to determine the relative risk for BIA-ALCL of various surface characteristics. Therefore, there is a need for an unambiguous, clinically validated classification system for breast implants including parameters beyond “surface roughness”. A history of textured breast implants/expanders appears to be necessary but is not sufficient for the development of BIA-ALCL. Contributing factors include, but are not limited to, a genetic predisposition to cancer and the presence of chronic inflammation, which may drive lymphomagenesis by multiple pathways.</p> <p>“The most important criterion that is associated with the occurrence of BIA-ALCL is the type of surface characterising the implant. Although the full aetiology is not yet understood, an appropriate control measure to reduce the identified risk is to limit the use of macro-textured implants, notably those prepared by the salt loss technique, and those with a certain type of PU coating.”</p>
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			in reconstructive surgery that involve either using autologous flap tissue or autologous fat transfer.	<p>The text on alternative implants has been modified.</p> <p>“The latter may need multiple procedures before an acceptable result is obtained. However, patients’ characteristics may limit the application of these techniques which are rarely used outside of reconstructive surgery practice.”</p>
52	Parreira Carlos, EASAPS ESAPS, Belgium	2.1 Answers to the Terms of References	<p>2.1.5. 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.</p> <p>SHEER report states line 22: “Based on a moderate weight of evidence, the SCHEER concludes that there is a causal relationship between textured breast implants and BIA-ALCL”.</p> <p>More correct is, as argued above: “Based on a moderate weight of evidence, the SCHEER concludes that there is a causal relationship between Biocell textured breast implants and BIA-ALCL”.</p> <p>Line 38: “Preventive explantation can be performed in cases of high risk” Too vague, be clear: “Preventive explantation can be performed in confirmed ALCL cases”</p> <p>Line 44: “However, some patients may request removal of the implant and capsule, particularly patients with manufacturer-recalled implants or the reported high-risk ISO macrot textured classification breast implants (e.g. polyurethane, salt-loss macrot textured, etc.). “ We are not aware of other high-risk Macrot textured implants being</p>	<p>SCHEER has considered the evidence and concluded that there is a moderate weight of evidence for a causal relationship between BIA-ALCL and textured breast implants. SCHEER has also identified the fact that the mechanism on the induction of BIA-ALCL by breast implants is not yet known, but considers local persistent inflammation as an important contributor.</p> <p>Text has been adapted on the textured implants:</p> <p>“Based on these data SCHEER considers that there is a moderate weight of evidence for a causal relationship between textured breast implants and BIA-ALCL, particularly in relation to implants with an intermediate to high surface roughness.</p> <p>At this point it should be noted that i) there are several types of textured implants ii) surface textures of breast implants are not all manufactured in the same way, and iii) implants with diverse surface textures may also present different benefits. The magnitude of the risk per type of textured implant is difficult to establish due to the low incidence of the risk. Even with macro-textured implants, BIA-ALCL has a very low incidence. Therefore, risk assessments per implant type are needed. Furthermore, the risk should be weighed against the benefits. There is also a need for an unambiguous, clinically validated classification system for breast implants including more parameters than just “surface roughness”. A history of textured breast implants/expanders appears to be necessary but not sufficient for the development of BIA-ALCL.”</p> <p>Line 38: In cases of confirmed BIA-ALCL, preventive explantation on</p>


			<p>consistently associated with BIA-ALCL in Europe so would prefer to leave the second part of this sentence out:  “However, some patients may request removal of the implant and capsule, particularly patients with manufacturer-recalled implants.”</p> <p>Line 49:  “In symptomatic patients with textured implants in place, implant removal with total capsulectomy is recommended. “  What is symptomatic? Having ALCL? Better:  “In ALCL diagnosed patients with textured implants in place, implant removal with total capsulectomy(preferrably en-bloc removal) is recommended. “</p>	<p>the contralateral implant is already indicated in the text.</p> <p>Line 44: Text has been modified:    “In non-symptomatic patients with textured implants or implants with unknown surface, implant removal with or without total capsulectomy for the single purpose of BIA-ALCL prophylaxis is not recommended due to the very low incidence of the disease. However, some patients may request removal of the implant and capsule, particularly patients with manufacturer-recalled implants or the reported high- breast implants (e.g. certain polyurethane, salt-loss macrot textured, etc.). Any surgery should follow an informed consent discussion on the related surgical risks and that a risk of BIA-ALCL may still persist. In symptomatic patients with textured implants in place, implant removal with total capsulectomy is recommended.”</p> <p>Line 49:  Indications for symptoms of BIA-ALCL are presented in the Opinion in section 4.4.2).</p>
53	Parreira Carlos, EASAPS and ESAPS, Belgium	2.1 Answers to the Terms of References	<p>2.1.1. To briefly describe what are the specific clinical indications and uses for various types of breast implants.</p> <p>In line 17 it is stated: “The clinical indications for the use of a specific type of breast implant do not depend on the preoperative clinical conditions, but only on the clinician’s and patient’s preferences, and consequently on industry and/or media information. “</p> <p>E(A)SAPS collection of opinions firmly disagrees with SCHEER’s statement that the influence of industry and media would prevail over the assessment of the surgeon when choosing a specific type of implant. On the contrary, it is our opinion that patient’s initial condition determines the best choice of implants for her specific expectation. Social media and representatives from the industry put pressure on our specialty but suggesting that non-scientific influencers determine our decisions is highly offensive to the integrity of aesthetic plastic surgeons in Europe and in the world in general. Replace line 17 with:</p>	<p>SCHEER agrees with this comment in that the choice of breast implant should not be driven by commercial aspects, but rather by the most appropriate implant for that specific patient with selection based on the most up-to-date scientific evidence available.</p> <p>Text adapted:    “The clinical indications for the use of a specific type of breast implant should depend on a consultation between clinician and patient to allow informed decision making to take place with regards to the choice of an appropriate breast implant. For breast reconstruction a shared consultation with a multidisciplinary healthcare team including a pathologist, oncologist, surgeon, breast care nurse, etc. should be held with the patient to allow informed decision making to take place with regards to the breast reconstruction procedure as well as the choice of implant. For both aesthetic and reconstructive surgery all aspects of breast implants should be evaluated and discussed with the patient, expressly covering advantages, disadvantages, follow-up</p>


		<p>“The clinical indications for the use of a specific type of breast implant depend on the preoperative clinical conditions as decided by the treating physician, not only on patient’s preferences, nor on industry and/or media information. “</p> <p>2.1.3. To indicate what is the state-of-the-art knowledge in terms of incidence of BIA- ALCL.  “The incidence of BIA-ALCL is considered low, varies by implant type, and is associated with textured implants. “  Not ALL textured implants, the majority is Biocell textured implants1. See joined reference where all cases were Biocell related. Please replace with:  “The incidence of BIA-ALCL is considered low, varies by implant type, and is associated with Biocell textured implants. “</p> <p>Ref 1 Trente-six cas français de lymphomes anaplasiques à grandes cellules associés aux implants mammaires. Que savons-nous sur leur histoire prothétique ? Thirty-six (36) French cases of Breast Implant-Associated Anaplastic Large Cell Lymphoma (BIA-ALCL): What do we know about their prosthetic histories, and what conclusions may be drawn?</p> <p>L.RuffenachC.Bruant-RodierF.GoldammerE.RamelliF.BodinC.Dissaux  Annales de Chirurgie Plastique Esthétique, Volume 64, Issue 4, August 2019, Pages 285-292 Doi : 10.1016/j.anplas.2019.05.002  “The estimation of the lifetime incidence of BIA- ALCL in women with implants has increased as presented in initial reports from 1 per million to current overall estimates of approximately 1 per 3000 women in Australia and the Netherlands.”</p> <p>This is suggestive that now the incidence is that high, while this is only in 2 countries. Better:  “The estimation of the lifetime incidence of BIA- ALCL in women with implants has increased significantly over the last years. Initial reports state 1 per million, and now in two countries (Australia and the Netherlands) it has increased to 1 per 3000 women. “</p>	<p>procedures and risk factors.”</p> <p>2.1 Q5. Text has been adapted on the textured implants:</p> <p>“Based on these data SCHEER considers that there is a moderate weight of evidence for a causal relationship between textured breast implants and BIA-ALCL, particularly in relation to implants with an intermediate to high surface roughness.</p> <p>At this point it should be noted that i) there are several types of textured implants ii) surface textures of breast implants are not all manufactured in the same way, and iii) implants with diverse surface textures may also present different benefits. The magnitude of the risk per type of textured implant is difficult to establish due to the low incidence of the risk. Even with macro-textured implants, BIA-ALCL has a very low incidence. Therefore, risk assessments per implant type are needed. Furthermore, the risk should be weighed against the benefits. There is also a need for an unambiguous, clinically validated classification system for breast implants including more parameters than just “surface roughness”. A history of textured breast implants/expanders appears to be necessary but not sufficient for the development of BIA-ALCL.”</p> <p>SCHEER has changed the text:</p> <p>“The estimation of the lifetime incidence of BIA-ALCL in women with implants has increased as presented in initial reports from 1 per million to current highest estimates of approximately 1 per 3000 women in Australia and the Netherlands.”</p>
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54	Jecan Cristian Radu, Romanian Association of Plastic Surgeons, Romania	2.1 Answers to the Terms of References	<p>page 11 - lines 12 - 13 RoAPS supports E(A)SAPS statement and comments - SCHEER concluded that “an appropriate control to reduce the identified risk is to limit the use of textured implants”. Unfortunately, the committee does not advise on the negative consequences of removing all textured implants from the market, such as risk for capsular contracture in sub-glandular position, animation deformity, distortion, double contour deformities, malposition, increased need of mesh, unfavorable results in conditions such as congenital deformities of the breast or after massive weight loss and especially breast reconstruction, to mention some examples. A restriction to smooth implants only sets the patient at a today not objectively evaluated risk for revision surgery. As well as this, all revision surgery has the inherent risk of complications, which is higher when capsulectomy is done. The outcome of such a report could lead to unnecessary worry in patients who are perfectly happy with their results demanding revision surgery. This, while there is no evidence based apparent advantage of such a procedure compared to mere observation, is likely to produce some unhappy patients after revision surgery.</p> <p>The SCHEER statement on the insufficient actual classification of shell texture is unanimously agreed upon in our community. E(A)SAPS would like to forward the opinion that a reliable definition of texture should include the following factors: shell shedding particles, friction and adhesivity factors besides the roughness of the shell.</p>	<p>Text on textured implants has been modified. SCHEER has considered the evidence and concluded that there is a moderate weight of evidence for a causal relationship between BIA-ALCL and textured breast implants. SCHEER has also identified the fact that the mechanism on the induction of BIA-ALCL by breast implants is not yet known, but considers local persistent inflammation as an important contributor.</p> <p>Text has been adapted on the textured implants:</p> <p>“Based on these data SCHEER considers that there is a moderate weight of evidence for a causal relationship between textured breast implants and BIA-ALCL, particularly in relation to implants with an intermediate to high surface roughness.</p> <p>At this point it should be noted that i) there are several types of textured implants ii) surface textures of breast implants are not all manufactured in the same way, and iii) implants with diverse surface textures may also present different benefits. The magnitude of the risk per type of textured implant is difficult to establish due to the low incidence of the risk. Even with macro-textured implants, BIA-ALCL has a very low incidence. Therefore, risk assessments per implant type are needed. Furthermore, the risk should be weighed against the benefits. There is also a need for an unambiguous, clinically validated classification system for breast implants including more parameters than just “surface roughness”. A history of textured breast implants/expanders appears to be necessary but not sufficient for the development of BIA-ALCL.”</p> <p>The SCHEER agrees with the comment that the surface characterization-classification of breast implants needs to be extended beyond roughness only.</p>
55	Jecan Cristain Radu, Romanian Association of	2.1 Answers to the Terms	<p>page 9 - lines 17,18,19 RoAPS supports E(A)SAPS collection of opinions firmly disagrees with SCHEER’s statement that the influence of industry and media would</p>	<p>SCHEER agrees with this comment in that the choice of breast implant should not be driven by commercial aspects, but rather by the most appropriate implant for that specific patient with selection based on</p>



	Plastic Surgeons, Romania	of References	<p>prevail over the assessment of the surgeon when choosing a specific type of implant. On the contrary, it is our opinion that patient’s initial condition determines the best choice of implants for her specific expectation. Social media and representatives from the industry put pressure on our specialty but suggesting that non-scientific influencers determine our decisions is highly offensive to the integrity of aesthetic plastic surgeons in Europe and in the world in general.</p> <p>The present SCHEER report does not provide useful recommendations on the surveillance of patients with all types of textured implants. Neither is it stated how to inform and advise patients presenting with implant related symptoms. It would be very helpful to add recommendations based on actual scientific data on the extent of capsular revision needed when patients request the removal of implants. The potential risk for developing BIA-ALCL is not known in cases with removal of textured implants but leaving remaining remnants of capsule. This fact has not been addressed and needs further research. E(A)SAPS opinion recommends that it could be advisable to investigate and analyse capsular samples removed from symptomatic patients at a centralized European university site.</p>	<p>the most up-to-date scientific evidence available</p> <p>Text adapted:</p> <p>“Clinical indications for the use of a specific type of breast implant should depend on a consultation between clinician and patient to allow informed decision making to take place with regards to the choice of an appropriate breast implant. For breast reconstruction a shared consultation with a multidisciplinary healthcare team including a pathologist, oncologist, surgeon, breast care nurse, etc should be held with the patient to allow informed decision making to take place with regards to the breast reconstruction procedure as well as the choice of implant. For both aesthetic and reconstructive surgery all aspects of breast implants should be evaluated and discussed with the patient, expressly covering advantages, disadvantages, follow-up procedures and risk factors.</p> <p>SCHEER has indicated in the Opinion when implant removal can be considered. The text on prophylactic removal of breast implants has been modified:</p> <p>“In non-symptomatic patients with textured implants or implants with unknown surface, implant removal with or without total capsulectomy for the single purpose of BIA-ALCL prophylaxis is not recommended due to the very low incidence of the disease. However, some patients may request removal of the implant and capsule, particularly patients with manufacturer-recalled implants or the reported high-risk breast implants (e.g. certain polyurethane, salt-loss macrot textured, etc.). Any surgery should follow an informed consent discussion on the related surgical risks and that a risk of BIA-ALCL may still persist. In symptomatic patients with textured implants in place, implant removal with total capsulectomy is recommended.”</p>
56	fischer thomas, swiss society of plastic reconstructive	2.1 Answers to the Terms of	2.1.1 the clinical indication for the use of a specific tipe DOES DEPEND ON THE PREOPERATIVE CLINICAL CONDITION:	<p>SCHEER agrees with this comment in that the choice of breast implant should not be driven by commercial aspects, but rather by the most appropriate implant for that specific patient with selection based on the most up-to-date scientific evidence available</p>

	and aesthetic surgery, switzerland	References	to achieve a natural reconstruction result: a slim or superslim patient needs absolutely a different type of Implant than a "Rubens like" built women. Industry doesn't have an influence on this at all: its all about shape, consistence and demension of the implant.	Text adapted:  "Clinical indications for the use of a specific type of breast implant should depend on a consultation between clinician and patient to allow informed decision making to take place with regards to the choice of an appropriate breast implant. For breast reconstruction a shared consultation with a multidisciplinary healthcare team including a pathologist, oncologist, surgeon, breast care nurse, etc. should be held with the patient to allow informed decision making to take place with regards to the breast reconstruction procedure as well as the choice of implant. For both aesthetic and reconstructive surgery all aspects of breast implants should be evaluated and discussed with the patient, expressly covering advantages, disadvantages, follow-up procedures and risk factors."
57	Barbara - Paolo Cagli - Montemurro, University Campus Bio Medico of Rome - Akademikliniken Stockholm Sweden , Italy	2.1 Answers to the Terms of References	<p>"the clinical indications for the use of a specific type of breast implant do not depend on the preoperative clinical conditions, but only on the clinician's and patient's preferences, and consequently on industry and/or media information". 2.1 Answers to the Terms of References (17-18-19-20)</p>  <p>CagliMontemurro_Comment_Scheer__3_.f</p> <p>"there are several alternatives to breast implants that involve plastic surgery techniques, either using autologous flap tissue or autologous fat transfer". 7. In the context of ALCL to briefly describe alternatives to breast implants. (17-18-19)</p>	<p>SCHEER agrees with this comment in that the choice of breast implant should not be driven by commercial aspects, but rather by the most appropriate implant for that specific patient with selection based on the most up-to-date scientific evidence available.</p> <p>Text adapted:</p> <p>"Clinical indications for the use of a specific type of breast implant should depend on a consultation between clinician and patient to allow informed decision making to take place with regards to the choice of an appropriate breast implant. For breast reconstruction a shared consultation with a multidisciplinary healthcare team including a pathologist, oncologist, surgeon, breast care nurse, etc should be held with the patient to allow informed decision making to take place with regards to the breast reconstruction procedure as well as the choice of implant. For both aesthetic and reconstructive surgery all aspects of breast implants should be evaluated and discussed with the patient, expressly covering advantages, disadvantages, follow-up procedures and risk factors.</p> <p>The text on alternative implants has been modified:</p>

				<p>“ The latter may need multiple procedures before an acceptable result is obtained. However, patients’ characteristics may limit the application of these techniques and these techniques are rarely used outside of reconstructive surgery. “</p>
58	Cardoso Maria-Joao, Eusoma (European Society of Breast Cancer Specialists), Italy	2.1 Answers to the Terms of References	<p>page 9 lines 49-52 page 11 lines12-13;31</p>  <p>scheer_o_018Eusoma comments.pdf</p>	<p>ALCL and BIA-ALCL are discussed as two separate entities in the text. See section 4.4.1 and 4.4.2.</p> <p>The comment on rarity of BIA-ALCL refers to the text in the Mandate. The Mandate of the Commission is an officially published EU document and as such cannot be modified.</p> <p>The rarity or uncommon presence of BIA-ALCL is indicated by the numbers. However, SCHEER agrees with the statement that BIA-ALCL is a rare (uncommon) disease, and considers that because approximately 1100 cases of BIA-ALCL are currently known (Clemens MW, 2nd World Consensus Conference on BIA-ALCL, 6-7 November 2020, Houston, Tx, USA), and because millions of women have breast implants, the prevalence of BIA-ALCL can be regarded as low.</p> <p>The comment on use textured versus smooth refers to the text in the Mandate. The Mandate of the Commission is an officially published EU document and as such cannot be modified. But so far, for almost all (probably with the exception of one) implants of which the surface characteristic was known, it was identified as textured.</p> <p>Q3 highest estimate of BIA-ALCL. As stated above. But so far, for almost all (probably with the exception of one) implants of which the surface characteristic was known, it was identified as textured.</p>

				<p>Q6 factors associated with BIA-ALCL. See above. So far, for almost all (probably with the exception of one) implants of which the surface characteristic was known, it was identified as textured.</p> <p>Text added page 2 Line 23, Page 8 line 35, Page 11 Q6: “A history of textured breast implants/expanders appears to be necessary but not sufficient for the development of BIA-ALCL.”</p> <p>Q8 what minimum data would be required. SCHEER has indicated the UDI (Unique Device Identification) number as basis. Further data to be collected should be agreed upon by clinicians, data managers and manufacturers.</p> <p>The choice of the patient or rather the consultation between clinician and patient has been addressed as follows in the text as answer to Question 1.</p> <p>“Clinical indications for the use of a specific type of breast implant should depend on a consultation between clinician and patient to allow informed decision making to take place with regards to the choice of an appropriate breast implant. For breast reconstruction a shared consultation with a multidisciplinary healthcare team including a pathologist, oncologist, surgeon, breast care nurse, etc should be held with the patient to allow informed decision making to take place with regards to the breast reconstruction procedure as well as the choice of implant. For both aesthetic and reconstructive surgery all aspects of breast implants should be evaluated and discussed with the patient, expressly covering advantages, disadvantages, follow-up procedures and risk factors.”</p> <p>See answer above on consultation between clinician and patient.</p>
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			<p>Heading of 4.4.2 by itself includes description and diagnosis. However, sub-sections have been added.</p> <p>Comment on spontaneous regression. Text in 4.5 modified:  “Based on the epidemiology, it was suggested that the uncommon occurrence of BIA-ALCL might be a consequence of spontaneous regression/resolution of the disease (Fleming et al., 2018, 2020, 2020). Of note, cases described by Fleming et al., as spontaneously regressing were treated, and only reduced numbers of BIA-ALCL cell numbers were observed rather than a complete absence. In general, BIA-ALCL has a favourable prognosis (Clemens et al. 2016, 2018).</p> <p>Fleming D, Stone J, Tansley P. Spontaneous Regression and Resolution of Breast Implant-Associated Anaplastic Large Cell Lymphoma: Implications for Research, Diagnosis and Clinical Management. <i>Aesthetic Plast Surg.</i> 2018 Jun;42(3):672-678. doi: 10.1007/s00266-017-1064-z. Epub 2018 Feb 14.</p> <p>Fleming D, Stone J, Tansley P. Spontaneous Regression and Resolution of Breast Implant-Associated Anaplastic Large Cell Lymphoma: Implications for Research, Diagnosis and Clinical Management. <i>Aesthetic Plast Surg.</i> 2020 Aug;44(4):1109-1115. doi: 10.1007/s00266-020-01810-2. Epub 2020 Aug 5.</p> <p>Fleming D, Stone J, Tansley P. Update: Spontaneous Regression and Resolution of Breast Implant-Associated Anaplastic Large Cell Lymphoma—Implications for Research, Diagnosis and Clinical Management—Our Reflections and Current Thoughts Two Years On. <i>Aesth Plast Surg</i> (2020) 44:1116–1119</p> <p>As with the choice of implant to be used (or procedure), consultation between clinician and patient is necessary.</p>
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59	Mercer Nigel, Plastic, Reconstructive and Aesthetic Expert Advisory Group (PRASEAG), United Kingdom	2.1 Answers to the Terms of References	<p>P9 Line 14-20: The indications for use of breast implants. This section could be explained better – perhaps as a summary of section 4.1. This section is very difficult to understand unless the reader has expert knowledge regarding implant usage. It also uses an idiosyncratic classification for implant usage of ‘primary’, ‘secondary’ and ‘aesthetic’</p> <p>P9 Line 35: Samples required for diagnosis of capsular invasion should be referenced in this section, as well as later.</p> <p>P9 Line 46: Varies by implant type and is associated with textured implants – This is confusing statement. Does it refer to different manufacturers, different implant type or different surface texture or all three? Evidence must be quoted for each such statement.</p> <p>P10 Line 9-11 ISO 14607 Implant surface roughness classification. The classification system used by each manufacturer should be tabulated. The using of different systems means that comparison of results between implants is scientifically flawed. It is like comparing ‘apples and pears’.</p> <p>P10 Line 22-33 very repetitive regarding potential causative factors.</p> <p>P10 5 para 3. The pros and cons of implant removal and total capsulectomy should also be discussed with the ‘worried well’ if, after a full explanation of BIA-ALCL they wish to have their implants removed, explaining that capsules should not be left behind and the increased morbidity associated with a total capsulectomy. There have been 2 reported cases of BIA-ALCL in retained capsules after implant removal and so a complete capsulectomy should be recommended with any implant removal/exchange.</p> <p>P11 Line 5-6 “The factor that determines the risk of BIA-ALCL is the presence of a breast implant, particularly a textured implant.</p> <p>P11 Line 7: What is meant by ‘genetic predisposition’ to cancer? This is</p>	<p>Q1. P9 Line 14-20. Text has been expanded to include consultation between clinician and patient on implant choice.</p> <p>Q2. Page 9 Line 35. Text modified. Appropriate extensive sampling of the capsule is required when evaluating for capsular invasion post-capsulectomy to determine disease free margins.</p> <p>Page 9 Line 46. All commented issues apply. This is stated in the main body text (section 4.4.2, 4.5, and 4.6) in which also reference is made to the literature.</p> <p>Page 10 Line 9-11. Only the generally accepted and published classifications are cited. The most important conclusion is that the main classification being used today, the ISO classification of implants based on surface roughness, is no longer considered sufficient, as also indicated by the TGA 2019 report.</p> <p>Page 10 Line 22-23. In this section, the specific question, as presented in the Mandate, has been answered:</p> <p>Q2. Page 10 Line 5 para 3. SCHEER recommends complete capsule removal as presented in Page 10 Line 39-40 of paragraph 3 for contralateral implants when BIA-ALCL is diagnosed in one implant. The recommendation for complete implant + capsule removal is stated in answer to Question 2 of the Mandate page 9 Line 36-39. “Therapeutic implant removal with a radical en bloc surgical resection, including total capsulectomy and eventual mass with safe oncologic margins of healthy tissue, is recommended as the state-of-the-art treatment, with a very good prognosis when the disease is promptly diagnosed at early stages.”</p>

		<p>a very important statement and needs to be explained.</p> <p>P11 Line 8: What is meant by the ‘presence of chronic inflammation’: This term needs to be explained and specified.</p> <p>P11 Line 12: Is it reasonable to limit the use of textured implant as a control measure given the stated incidence is ‘very low’? The impact of using only smooth implants will create new problems that are likely to exceed the risks the ‘control measure’ is trying to avoid.</p> <p>P11 Line 5-13: The report states that the use of textured implants should be limited as a ‘control measure’ but later suggests it should be a matter for informed consent and patient choice. For example, HRT is not banned despite it having much greater risk if cancer than the use of a breast implant. Smoking is not banned despite it having no benefits at all. Why should textured breast implants be limited as a control measure? It is the patient who needs to decide if they will accept one, knowing all the risks and benefits.</p> <p>Patient choice is paramount and they must be given the pros and cons of every procedure that may be applicable to them and their condition so that they can may a ‘shared decision’. We left the days where the ‘surgeon knows best’ many years ago in Europe.</p> <p>P11 Line 35: In an ideal world, industry should not fund the BCIR and it should be funded by taxation but why should companies sell products that are under researched and not contribute in some way to the costs of manufacturing failures, even if these are unintentional/unforeseeable? A levy should be charged on the sale of each and every implant sold for human use (including breast implants) to fund the central collection of data independent of the companies who produce and sell them.</p>	<p>Q6 Page 11 Line 5-6. Text has been modified.  “The factor that determines the risk of BIA-ALCL is the presence of an implant with a textured or rough surface, i.e. not smooth surface,. In addition, a certain type of PU implant manufacturing process might also result in a risk for BIA-ALCL. However, it is not yet possible to determine the relative risk for BIA-ALCL of various surface characteristics. Therefore, there is a need for an unambiguous, clinically validated classification system for breast implants including more parameters than just “surface roughness”.</p> <p>Q6. Page 11 Line 7. Genetic predisposition is explained in the main body text on page 32 section 6.4 in which indications for genetic factors that might be involved in BIA-ALCL are mentioned.</p> <p>Q6. Page 11 Line 8. The presence of chronic inflammation is presented in section 6.4. Mediating and/or moderating factors associated with the risk of BIA-ALCL.</p> <p>Q6. Page 11 Lin 12. Text on textured implants is modified and now more specific.  “Although the full aetiology is not yet understood, an appropriate control measure to reduce the identified risk is to limit the use of macro-textured implants, notably those prepared by the salt loss technique, and those with a certain type of PU coating.”</p> <p>Page 11 Line 5-13. Text on choice of implant has been modified and now indicates importance of consultation between clinician and patient. In answer to Question 1:  “Clinical indications for the use of a specific type of breast implant should depend on a consultation between clinician and patient to allow informed decision making to take place with regards to the choice of an appropriate breast implant. For breast reconstruction a shared consultation with a multidisciplinary healthcare team including a pathologist, oncologist, surgeon, breast care nurse, etc should be held with the patient to allow informed decision making to take place with regards to the breast reconstruction procedure as well as the choice of implant. For both aesthetic and reconstructive surgery all</p>
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				<p>aspects of breast implants should be evaluated and discussed with the patient, expressly covering advantages, disadvantages, follow-up procedures and risk factors.”</p> <p>Page 11 Line 35. SCHEER considers independent funding for registries essential in order to avoid any influence of industry on the registration characteristics and process. It might be raised through a tax on the sale of implants, but that is not in the remit of SCHEER, but for government to decide.</p>
60	Decaluwé Kelly, The Federal Agency of Medicines and Health Products, Belgium	2.1 Answers to the Terms of References	<p>Page 11, line 52 - 53</p> <p>An equally important subject for future research is treatment optimization, especially for the more advanced disease stages.</p>	<p>BIA-ALCL in general has a good prognosis. It is outside the remit of SCHEER to discuss extensive treatment modalities for various stages of BIA-ALCL</p>
61	Decaluwé Kelly, The Federal Agency of Medicines and Health Products, Belgium	2.1 Answers to the Terms of References	<p>Page 11, line 46 - 47</p> <p>It is suggested within the report that implants exposed to an in vivo environment (i.e. explants) should be evaluated for surface characteristics.</p> <p>Who would be responsible for this investigation? Is the implant manufacturer's responsibility or should this rather be done by one or more research groups? Should the focus be only on the implant and its surface characteristics following revision surgery or should capsules be analysed too in order to identify potential bio-compatibility issues?</p>	<p>Research to be conducted is up to the research community itself. All issues mention in the comment might be of interest to study.</p>
62	Decaluwé Kelly, The Federal Agency of Medicines and Health Products, Belgium	2.1 Answers to the Terms of References	<p>Page 11, Line 30 - 34</p> <p>Aiming for an EU based registry or at least a minimum harmonised dataset for all EU countries would allow maximum uniformity. Furthermore, in order for competent authorities to be able to take appropriate measures in a timely manner, EU member states should be able to gain access to these registries or at least receive periodic reports while respecting the privacy rules.</p>	<p>SCHEER agrees with the comment but it is for the EU MS to implement such registries. Globally a start has been made with the International Collaboration of Breast Registry Activities (ICOBRA) (Cooter et al, 2015).</p>
63	CAMPANALE	2.1	<p>p. 9 line 17-20: According to the feedback received from the Expert</p>	<p>Page 9 Line 17-20</p>



	ANTONELLA, ITALIAN MINISTRY OF HEALTH, Italy	Answers to the Terms of References	<p>group established at the IMoH and from National Scientific Associations (SICPRE and AICPE), the clinical indication for the use of one type of breast implant versus another type DEPENDS on the preoperative clinical condition for both aesthetic and reconstruction purposes. Moreover, this sentence is contradictory with the sentence reported in the paragraph 4.3 ALTERNATIVES TO BREAST IMPLANTS at page 15 line 33-40.</p> <p>p. 9 line 45 -49: To date the estimated incidence worldwide has a significant VARIABILITY that is attributable to all the factors that influence the numerator and the denominator in each country. The estimated values are not comparable because calculated differently and with several different limitations. Therefore, the statements that the incidence is increased is inaccurate. Although THERE HAS BEEN AN INCREASE IN THE number of cases, thanks to the raised awareness and to all the actions undertaken at National level, we believe that THE monitoring incidence rate per year is fundamental. In our experience where the method used to estimate the incidence is homogeneous, we observed that although small oscillations were observed between 2015 and 2018, these are not statistically significant, and the disease remains a rare disorder with an incidence of about 3/100.000 implanted patients per year (Campanale 2020)</p> <p>p.10 line 22-24:According to the definition of MODERATE weight of evidence (SEE SCHEER WoE, 2018) “there are good evidences from a primary line of evidence”. Please give more details and explanations about these primary lines of evidences referring to causal relationship between textured breast implants and BIA-ALCL.</p> <p>p. 10 line 35-37: We agree with this sentence and we would like to stress that it needs to be reminded for every case independently from the device found at the time of diagnosis.</p> <p>p. 10 line 37-41: We agree with this sentence but we would like to highlight that this statement is contradictory with that reported at page 21, line 54-55, where the possibility of an immediate reconstruction with smooth implant would be possible. This sentence of the</p>	<p>Text on implant choice has been modified:  ““Clinical indications for the use of a specific type of breast implant should depend on a consultation between clinician and patient to allow informed decision making to take place with regards to the choice of an appropriate breast implant. For breast reconstruction a shared consultation with a multidisciplinary healthcare team including a pathologist, oncologist, surgeon, breast care nurse, etc should be held with the patient to allow informed decision making to take place with regards to the breast reconstruction procedure as well as the choice of implant. For both aesthetic and reconstructive surgery all aspects of breast implants should be evaluated and discussed with the patient, expressly covering advantages, disadvantages, follow-up procedures and risk factors.”</p> <p>Page 9 Line 45-49.  SCHEER agrees with the comment that there are differences in the reported incidences that are dependent on the methodology used.</p> <p>SCHEER considers the fact that, for almost all implants (probably with the exception of one) of which the surface characteristic was known, it was identified as textured. In addition, a certain type of PU implant manufacturing process might also result in a risk for BIA-ALCL.</p> <p>Page 10 Line 35-37. SCHEER thanks Dr Campanale for the comment.</p> <p>Page 21 Line 54-55. The text has been modified and the word “smooth” has been deleted.</p> <p>“After surgery for BIA-ALCL, immediate or delayed breast reconstruction or further augmentation has been reported using implants or autologous tissue (Lamaris et al., 2019). The patient needs to be fully informed regarding current uncertainty about the safety of various types of breast implants with regards to BIA-ALCL and capsule formation.</p> <p>Page 11 Line 5-6. Text modified as follows:</p>
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			<p>preliminary opinion might send the wrong message that smooth implants are certainly safe and excluded from the pathogenesis of this disease and can be implanted also in high risk patients.</p> <p>p. 11 line 5-6: As far as we are concerned, this is a wrong and dangerous sentence since the WG excludes beyond any reasonable doubt smooth implants as a possible risk factor of developing BIA-ALCL.</p> <p>p. 11 line 11-13: Such type of decisions on the risk management should be taken after an accurate and overall risk/benefit ratio evaluation for textured and smooth devices. As more than 95% of breast prostheses implanted in Italy are textured, the IMoH has collected sufficient data from vigilance and post-market surveillance about these types of devices and, as a result, we do not have sufficient data about smooth devices. We are unable to estimate the mean lifetime of a smooth implant and we are unable to evaluate their risk/benefit ratio. Moreover, taking into account the lack of data (problem that occurs to the FDA as well), we believe that the above-mentioned sentence is not correct.</p>	<p>“The factor that determines the risk of BIA-ALCL is the presence of an implant with a textured or rough surface, i.e. not smooth surface,. In addition, a certain type of PU implant manufacturing process might also result in a risk for BIA-ALCL. However, it is not yet possible to determine the relative risk for BIA-ALCL of various surface characteristics. Therefore, there is a need for an unambiguous, clinically validated classification system for breast implants including more parameters than just “surface roughness”.</p> <p>Page 11 line 11-13. Text modified.  “The full aetiology of BIA-ALCL is not yet understood, although an appropriate control measure to reduce the identified risk, is to limit the use of macro-textured implants, notably those prepared by the salt loss technique, and those with a certain type of PU coating.”</p>
64	Garson Sebastien, SNCPRE SOFCEP, France	2.1 Answers to the Terms of References	<p>Page 11 line 12:  Our society show the rate of lost of chance especially in breast reconstruction 73% after the unilateral ban of the texture implant in France.  We hope Europe will be smarter than France in their conclusion and decision.  Talking Texture in a same bag is a poor non scientific approach. Please take the time to analyses all the data with the same accurate filter.  If you do so you will found the number one prob is the Biocel® by far .For the other texturation it will be high inflammatory capsula reaction for salt macrotexuration, less for vulcanisation, less for sugar macro texturation, less for imprint macro and more less for the sugar micro and very low or none inflammatory capsula reaction for imprint micro.  We have seen with the French data that almost 100% of the BIA ALCL with the full patient story get an exposure in their live to the Biocel® Allergan®.  Your paper doesn't mention the capsula memory.</p>	<p>Text on page 11 line 12 is modified.  “The full aetiology of BIA-ALCL is not yet understood, although an appropriate control measure to reduce the identified risk, is to limit the use of macro-textured implants, notably those prepared by the salt loss technique, and those with a certain type of PU coating.”</p> <p>Based on epidemiology the text of the conclusion in section 6.2. was expanded by the sentence.  “As far as the manufacturer for textured implants was known most cases were found for the Biocell implant (texture manufactured by salt loss technique), while for PU coated breast implants BIA-ALCL cases were mainly associated with Silimed implants. Cases for other manufacturers were much lower.”</p>

65	BENITO-RUIZ JESUS, ANTIAGING GROUP BARCELONA, Spain	2.1 Answers to the Terms of References	LINES 17 TO 19 Comment: The selection of implants are based on breast (fingerprint of the breast, shape, ptosis) and chest characteristics. The diagnosis (breast absence, amastia, tuberous breast and even in pure aesthetic cases for changes of volume and shape) is paramount to choose the proper implant (shape and volume). The final decision is clinical judgment first. This is matched with patient desires as much as possible. This is key to prevent complications such as waterfall deformity, rippling, double fold, dynamic breast, etc.	Q1. Text modified to emphasize choice of implant related to patient characteristics.  “Clinical indications for the use of a specific type of breast implant should depend on a consultation between clinician and patient to allow informed decision making to take place with regards to the choice of an appropriate breast implant. For breast reconstruction a shared consultation with a multidisciplinary healthcare team including a pathologist, oncologist, surgeon, breast care nurse, etc should be held with the patient to allow informed decision making to take place with regards to the breast reconstruction procedure as well as the choice of implant. For both aesthetic and reconstructive surgery all aspects of breast implants should be evaluated and discussed with the patient, expressly covering advantages, disadvantages, follow-up procedures and risk factors.”
66	CIRILLO PIERFRANCESCO, AICPE ITALIAN ASSOCIATION OF AESTHETIC PLASTIC SURGERY, Italy	2.1 Answers to the Terms of References	Point 1: We think that to affirm that: "The clinical indications for the use of a specific type of breast implant do not depend on the preoperative clinical conditions, but only on the clinician's and patient's preferences, and consequently on industry and/or media information.", is scandalously offensive to plastic surgery and its history: to describe plastic surgeons as mere executors of requests made by patients or manufacturers is unbearable. We are clinicians and our decisions are made on the basis of a serious assessment and selection of patients. To state this, is seriously prejudicial and, on behalf of 430 Aicpe's Italian Plastic Surgeons, whom I represent as President, I formally invite you to modify these statements which are prejudicial and seriously damaging to a surgical specialty which does not deserve these superficial and scientifically incorrect conclusions.	Q1. Text modified to emphasize choice of implant related to patient characteristics.  “Clinical indications for the use of a specific type of breast implant should depend on a consultation between clinician and patient to allow informed decision making to take place with regards to the choice of an appropriate breast implant. For breast reconstruction a shared consultation with a multidisciplinary healthcare team including a pathologist, oncologist, surgeon, breast care nurse, etc should be held with the patient to allow informed decision making to take place with regards to the breast reconstruction procedure as well as the choice of implant. For both aesthetic and reconstructive surgery all aspects of breast implants should be evaluated and discussed with the patient, expressly covering advantages, disadvantages, follow-up procedures and risk factors.”
67	Sukop Andrej, Czech Society of Plastic Surgery, Czech Republic	3. MINORITY OPINION	In some countries, a mandatory breast implant registries exist. Very often though, they are not fully functional, sometimes due to the recently implemented GDPR rules. In the Czech Republic, an up-to-date registry of patients with ALCL should be established and the input of the	SCHEER agrees with the comment. However, SCHEER acts as scientific advisory body for the EC, and has no such function for Member States.

			information into the registry should be obligatory for the surgeon.	
68	De Mezerville Roberto, Establishment Labs, Costa Rica	4. INTRODUCTION	<p>COMMENT: It is stated that the response to different implant surfaces at a cellular level needs to be further studied to establish cellular response and biocompatibility.</p> <p>RECOMMENDATION: There has been extensive research and published evidence by authors like Barr, Hill &amp; Bayat; Atlan et al.; Valencia-Lazcano, Cappellano et al., and recently Hobson et al., that have already characterized differential immune response and biocompatibility to available commercial implants. These should be included as supporting evidence that is expected to have clinical relevance and correlation with chronic inflammatory risk. Attached some of the most well-known peer-reviewed studies on the subject.</p>	SCHEER disagrees with the statement to include the indicated literature in this general introduction section. Relevant literature is cited at appropriate places in the Opinion such as section 4.6 and section 6.4.
69	Geertsma Robert, RIVM - National Institute for Public Health and the Environment, Netherlands	4.1 Use of breast implants	<p>4.1 p.14, lines 1-3 While mentioned above, the summary does not mention the case of preventive surgery in women with a BRCA mutation.</p>	Text added to second bullet. "Secondary reconstruction following a previous surgical procedure after breast cancer or preventive surgery in women with BRCA mutation."
70	Sukop Andrej, Czech Society of Plastic Surgery, Czech Republic	4.1 Use of breast implants	<p>Use of anatomic breast implant is, in many cases, more convenient for the patient. The selection of the implant is made by a plastic surgeon according by his/her own experience, the wishes of the patient and the characteristics of patient's own tissue.</p> <p>Smooth implants present with a higher risk of capsular contracture and a higher risk of reoperation with all the possible consequences for the patient.</p>	Text modified to emphasize choice of implant related to patient characteristics.  "Some trends are apparent in the literature for the use of one or another type of breast implant. However, the clinical indications for the use of a specific type of breast implant should depend on a consultation between clinician and patient to allow informed decision making to take place with regards to the choice of an appropriate breast implant. For breast reconstruction a shared consultation with a multidisciplinary healthcare team including a pathologist, oncologist, surgeon, breast care nurse, etc. should be held with the patient to allow informed decision making to take place with regards to the breast reconstruction procedure as well as the choice of implant. For both aesthetic and reconstructive surgery all aspects of breast


				implants should be evaluated and discussed with the patient, expressly covering advantages, disadvantages, follow-up procedures and risk factors.”
71	Parreira Carlos, EASAPS ESAPS, Belgium	4.1 Use of breast implants	<p>4.1. Use of breast implants</p> <p>In line 46 it is stated:  “Some trends are apparent in the literature, although the clinical indications for the use of one type of breast implant versus another do not depend on the preoperative clinical conditions, but only on the clinician’s and patient’s preferences, and consequently information provided by industry and/or media information. “</p> <p>The SCHEER report states that “the choice of implants does not depend on the clinical condition, but instead on the clinician’s and patient’s preferences, and consequently information provided by industry and/or media sources.” E(A)SAPS collection of opinions firmly disagrees with SCHEER’s statement that the influence of industry and media would prevail over the assessment of the surgeon when choosing a specific type of implant. On the contrary, it is our opinion that patient’s initial condition determines the best choice of implants for her specific expectation. Social media and representatives from the industry put pressure on our specialty but suggesting that non-scientific influencers determine our decisions is highly offensive to the integrity of aesthetic plastic surgeons in Europe and in the world in general.</p> <p>The present SCHEER report does not provide useful recommendations on the surveillance of patients with all types of textured implants. Neither is it stated how to inform and advise patients presenting with implant related symptoms. It would be very helpful to add recommendations based on actual scientific data on the extent of capsular revision needed when patients request the removal of implants. The potential risk for developing BIA-ALCL is not known in cases with removal of textured implants but leaving remaining remnants of capsule. This fact has not been addressed and needs further research. E(A)SAPS opinion recommends that it could be advisable to investigate and analyse capsular samples removed from</p>	<p>Text modified to emphasize choice of implant related to patient characteristics.</p> <p>“Some trends are apparent in the literature for the use of one or another type of breast implant. However, the clinical indications for the use of a specific type of breast implant should depend on a consultation between clinician and patient to allow informed decision making to take place with regards to the choice of an appropriate breast implant. For breast reconstruction a shared consultation with a multidisciplinary healthcare team including a pathologist, oncologist, surgeon, breast care nurse, etc should be held with the patient to allow informed decision making to take place with regards to the breast reconstruction procedure as well as the choice of implant. For both aesthetic and reconstructive surgery all aspects of breast implants should be evaluated and discussed with the patient, expressly covering advantages, disadvantages, follow-up procedures and risk factors.”</p> <p>Regarding the surveillance and follow-up of patients, SCHEER strongly recommends a breast implant registry in which all aspects of the implant including clinical outcome (e.g. BIA-ALCL) should be included for possible further analysis. The individual follow-up of patients should be conducted according to local guidelines, for example as described in the NCCN report.</p>

			<p>symptomatic patients at a centralized European university site.</p> <p>Please change to:  “Some trends are apparent in the literature, although the clinical indications for the use of a specific type of breast implant depend on the preoperative clinical conditions as decided by the treating physician, not only on patient’s preferences, nor on industry and/or media information. “</p> <p>In line 28 it is correctly stated that the majority of breast implants are used for aesthetic reasons, why then are they put last in the summary in line 51? More logical would be:</p> <ul style="list-style-type: none"> <li>• Aesthetic use for increasing breast volume and improving its shape.</li> <li>• Secondary reconstruction following a previous surgical procedure</li> <li>• Primary Reconstruction, i.e., the replacement of breast volume lost after accidental or iatrogenic trauma, mastectomy for breast cancer, and developmental anatomic anomalies such as amastia, tuberous breast and Poland syndrome.</li> <li>• Correction of aesthetic variants such as hypomastia and anisomastia.</li> </ul>	<p>SCHEER has followed an order of necessity in listing breast implant use. Cosmetic applications, although the highest in use, is of the least medical necessity.</p>
72	<p>Handstein Steffen, Vereinigung der Deutschen Ästhetisch-Plastischen Chirurgen/German Association of Aesthetic-Plastic Surgeons, Germany</p>	<p>4.1 Use of breast implants</p>	<p>"Clinical indications for the use of breast implants are either reconstructive or aesthetic. Reconstructive surgery comprises approximately 25% of cases with the remaining 75% used for aesthetic reasons (Heidekrueger et al., 2018)." Regarding this the present SCHEER report 2020 has not reasonably represented the opinion of European aesthetic plastic surgeons and their scientific societies. Aspects of safety and objective information for aesthetic patients with breast implants are not sufficiently discussed.</p> <p>We absolutely disagree with SCHEER’s statement that the influence of industry and media would prevail over the assessment of the surgeon when choosing a specific type of implant. On the contrary the patients initial condition determines the best choice of implants for her specific expectation. There are certain differences in choosing an appropriate implant for reconstructive or aesthetic reasons. On the other hand the differentiation between aesthetic and reconstructive indications are not as clear as stated in the report. This might be highly dependent on</p>	<p>Regarding the lack of presentation of the view of European aesthetic surgeons. SCHEER comments the following: Expert selection was performed according to the Rules of procedures of the Scientific Committees. (<a href="https://ec.europa.eu/health/scientific_committees/docs/rules_procedure_2016_en.pdf">https://ec.europa.eu/health/scientific_committees/docs/rules_procedure_2016_en.pdf</a>).</p> <p>There was a public, open call for experts to participate in the respective working group formed by SCHEER (<a href="https://ec.europa.eu/health/scientific_committees/call_experts/call_experts_bia_alcl_en">https://ec.europa.eu/health/scientific_committees/call_experts/call_experts_bia_alcl_en</a>), the deadline of which was actually extended once (from December 4th, 2019 to January 3rd, 2020) due to the low response received from experts. Therefore all experts and their respective societies have had the opportunity to contribute towards the finalization of this Opinion during the public consultation period, and they did so by providing numerous comments, as detailed in this document.</p>

			different health care providers, i. e. national systems of insurance systems, as well as fiscal reasons in each country.	Text modified to emphasize choice of implant related to patient characteristics:  “Some trends are apparent in the literature for the use of one or another type of breast implant. However, the clinical indications for the use of a specific type of breast implant should depend on a consultation between clinician and patient to allow informed decision making to take place with regards to the choice of an appropriate breast implant. For breast reconstruction a shared consultation with a multidisciplinary healthcare team including a pathologist, oncologist, surgeon, breast care nurse, etc should be held with the patient to allow informed decision making to take place with regards to the breast reconstruction procedure as well as the choice of implant. For both aesthetic and reconstructive surgery all aspects of breast implants should be evaluated and discussed with the patient, expressly covering advantages, disadvantages, follow-up procedures and risk factors.”
73	Mercer Nigel, Plastic, Reconstructive and Aesthetic Expert Advisory Group, United Kingdom	4.1 Use of breast implants	<p>P13 Line 29: The reference Heidekrueger et al 2018 is incorrect. The paper, whilst interesting and well written, is based on a questionnaire: 25% reconstructive and 75% aesthetic surgeons NOT of implant use. It of course makes one question if all the other references quoted have been read by the authors or taken on trust.</p> <p>P13 Line 32: The use of the word ‘amputation’ for mastectomy is not acceptable. In addition, The term 'Breast mound’ is also very surgeon oriented and reflects what could be achieved in 1990 not 2020. The authors need to move away from a clearly paternalistic approach to patients to the 21st century position where the ‘reasonable patient’ makes choices about their care based on knowledge of the ‘material risks’ of the applicable procedures. Surgeon does not lone best.</p>	<p>P13 Line 29 Text modified to reflect better Heidekrueger et al. 2018, and reference added.</p> <p>“Reconstructive surgery comprises approximately 25% of cases with the remaining 75% used for aesthetic reasons, or may be evenly distributed depending on the geographical region as indicated by a survey under plastic surgeons (Heidekrueger et al., 2018, Loch-Wilkinson et al., 2020)</p> <p>P13 Line 36. Text modified.</p> <p>“Examples of implant use for reconstructive surgery include restoration of a breast following mastectomy (i.e. removal of the breast), treatment for breast cancer,.....”</p>



			<p>P13 Line 44: improving its shape: In suggesting that the natural shape of a breast can be 'improved', what scale of 'improvement' are they using? This would be better expressed as 'altering or adjusting' the breast shape.</p> <p>P13; Line 46-49: The pre-op choice of implant does not depend on 'preoperative clinical conditions' and better terminology should be used. The final choice of implant lies with the patient after full discussion with the surgeon about the pros and cons of what treatments are applicable.</p> <p>P13/14 Line 51 - 6: this is not an implant use classification that makes sense. See previous comments.</p>	<p>P13 Line 44. Text modified: ".....adjusting its shape."</p> <p>P13 Line 46-49. Text modified. "Some trends are apparent in the literature for the use of one or another type of breast implant. However, the clinical indications for the use of a specific type of breast implant should depend on a consultation between clinician and patient to allow informed decision making to take place with regards to the choice of an appropriate breast implant. For breast reconstruction a shared consultation with a multidisciplinary healthcare team including a pathologist, oncologist, surgeon, breast care nurse, etc., should be held with the patient to allow informed decision making to take place with regard to the breast reconstruction procedure as well as the choice of implant. For both aesthetic and reconstructive surgery all aspects of breast implants should be evaluated and discussed with the patient, expressly covering advantages, disadvantages, follow-up procedures and risk factors."</p> <p>P13/14 Line 51-6. This is not intended as a kind of classification. It is intended as a summing up of the various uses of a breast implant.</p>
74	CAMPANALE ANTONELLA, ITALIAN MINISTRY OF HEALTH, Italy	4.1 Use of breast implants	<p>p. 13 line 46-49: According to the feedback received from the Expert group established at the IMoH and from National Scientific Associations (SICPRE and AICPE), the clinical indication for the use of one type of breast implant versus another <b>DEPENDS</b> on the preoperative clinical condition for both aesthetic and reconstruction purposes and not on patient's preferences or information provided by industry and/or media sources</p>	<p>SCHEER agrees. Text has been modified:</p> <p>"Some trends are apparent in the literature for the use of one or another type of breast implant. However, the clinical indications for the use of a specific type of breast implant should depend on a consultation between clinician and patient to allow informed decision making to take place with regards to the choice of an appropriate breast implant. For breast reconstruction a shared consultation with a multidisciplinary healthcare team including a pathologist, oncologist, surgeon, breast care nurse, etc should be held with the patient to allow informed decision making to take place with regards to the breast reconstruction procedure as well as the choice of implant. For both aesthetic and reconstructive surgery all aspects of breast implants should be evaluated and discussed with the patient, expressly covering advantages, disadvantages, follow-up procedures</p>



75	MARTIN DEL YERRO JOSE LUIS, HOSPITAL UNIVERSITARIO QUIRÓN SALUD. UNIVERSIDAD EUROPEA DE MADRID. SPAIN, Spain	4.1 Use of breast implants	<p>Dear members of the Scientific Committee on Health, Environmental and Emerging Risks (SCHEER),</p> <p>We appreciate the work you have done in this preliminary opinion on the safety of breast implants related to BIA-ALCL, and we welcome your request to receive comments on it. We take this opportunity to share our thoughts after more than 27-year of experience using textured breast implants from Mentor, McGhan-Inamed-Allergan and Polytech.</p>  <p>Martin_del_Yerro_Plastic_Surgeons_comm</p>	<p>and risk factors.”</p> <p>Answer to the comments:</p> <ul style="list-style-type: none"> <li>- The text on implant choice has been adapted (see various other comments and answers above).</li> <li>- Text on implant surfaces has been adapted and now a more balanced view is presented (see various other comments and answers above).</li> <li>- In terms of proof of evidence, SCHEER considers the fact that almost (if not) all BIA-ALCL cases as far as implant surface was known, show a textured surface, is sufficient evidence to a role of the implant textured surface in the development of BIA-ALCL.</li> <li>-</li> </ul> <p>Text added in answer to Q5 and Q6.</p> <p>Q5: “Based on these data, SCHEER considers that there is a moderate weight of evidence for a causal relationship between textured breast implants and BIA-ALCL, particularly in relation to implants with an intermediate to high surface roughness.</p> <p>At this point it should be noted that i) there are several types of textured implants ii) surface textures of breast implants are not all manufactured in the same way, and iii) implants with diverse surface textures may also present different benefits. The magnitude of the risk per type of textured implant is difficult to establish due to the low incidence of the risk. Even with macro-textured implants, BIA-ALCL has a very low incidence. Therefore, risk assessments per implant type are needed. Furthermore, the risk should be weighed against the benefits. There is also a need for an unambiguous, clinically validated classification system for breast implants including more parameters than just “surface roughness”.; A history of textured breast implants/expanders appears to be necessary but not sufficient for the development of BIA-ALCL. Another risk factor for BIA-ALCL may be due to the manufacturing process for certain types of PU coating.”</p>
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				<p>Q6: “A history of textured breast implants/expanders appears to be necessary but not sufficient for the development of BIA-ALCL”</p> <p>It should be noted that in view of the lack of randomized clinical trials and the often lack of information on the denominator in the clinical studies a statistical approach and power analysis of BIA-ALCL incidences is not possible.</p>
76	BENITO-RUIZ JESUS, ANTIAGING GROUP BARCELONA, Spain	4.1 Use of breast implants	<p>lines 46-49</p> <p>Comment: The selection of implants are based on breast (fingerprint of the breast, shape, ptosis) and chest characteristics. The diagnosis (breast absence, amastia, tuberous breast and even in pure aesthetic cases for changes of volume and shape) is paramount to choose the proper implant (shape and volume). The final decision is clinical judgment first. This is matched with patient desires as much as possible. This is key to prevent complications such as waterfall deformity, rippling, double fold, dynamic breast, etc.</p>	<p>SCHEER agrees. Text has been modified:</p> <p>“Some trends are apparent in the literature for the use of one or another type of breast implant. However, the clinical indications for the use of a specific type of breast implant should depend on a consultation between clinician and patient to allow informed decision making to take place with regards to the choice of an appropriate breast implant. For breast reconstruction a shared consultation with a multidisciplinary healthcare team including a pathologist, oncologist, surgeon, breast care nurse, etc should be held with the patient to allow informed decision making to take place with regards to the breast reconstruction procedure as well as the choice of implant. For both aesthetic and reconstructive surgery all aspects of breast implants should be evaluated and discussed with the patient, expressly covering advantages, disadvantages, follow-up procedures and risk factors.”</p>
77	Geertsma Robert, RIVM - National Institute for Public Health and the Environment, Netherlands	4.2 Types of breast implants	<p>4.2 Lines 44-48</p> <p>Wrong terminology in line 44: should be “coated:” instead of textured; “attempt to reduce complications” – this should be elaborated on: does it work?</p>	<p>SCHEER agrees. Text adapted.</p> <p>The word “textured” has been replaced by “coated”.</p>
78	No agreement to disclose personal	4.2 Types of breast	Please refer to the attached document	SCHEER has taken notice of the document that contained comments addressing practices of plastic surgeons. These comments were


	data	implants		therefore considered not relevant to the text of the Opinion itself.
79	No agreement to disclose personal data	4.2 Types of breast implants	<p>General comment Why have scientific assessments on surface characterisation such as the TGA Biomaterials and Engineering Laboratory Report: Non-active mammary implants, not been cited? This has a scientific method for surface characterisation.  <a href="https://www.tga.gov.au/biomaterials-and-engineering-laboratory-report-non-active-mammary-implants">https://www.tga.gov.au/biomaterials-and-engineering-laboratory-report-non-active-mammary-implants</a></p>	<p>Text on surface assessment has been modified and the TGA report has now been included in section 4.6.</p> <p>“A recent TGA report has evaluated breast implants on the Australian market. (TGA 2019). The TGA concluded that the ISO method did not adequately describe the complexities of surface textures resulting from the myriad of texturing techniques manufacturers employ. Additionally TGA employed micro-Computed Tomography to extend the categories for surface characterization and was therefore able to group breast implants according to surface characteristics. These groupings include polyurethane-coated, closed salt-loss, open salt-loss, imprinting, subsurface gas diffusion, surface gas diffusion and smooth. It was concluded that the current classification systems require refinement and further examination to develop practical and clinical applications.”</p> <p>And</p> <p>“. The ISO 14607:2018 is currently under revision as the classification based on surface roughness only was considered too limited as was also concluded in the TGA 2019 report.”</p>
80	MAYO MARTÍN FEDERICO, PLASTIC SURGEON PRIVATE PRACTICE ZÜRICH- MADRID, Spain	4.2 Types of breast implants	<p>All the text is related to a type of breast implant, and the alternative to textured ones, an EU approved smooth anatomical implant , without the possible complications of the textured ones, like BIA-ALCL.</p> <p>Anatomical and smooth option is called Motiva Anatomical True Fixation, Available at the European Union. It is an smooth surface implant, and form stable one, without any reported case of double capsula, late seroma or BIA-ALCL.</p>	<p>SCHEER does not mention all companies with a breast implant on the market. Regarding the relationship between textured implants and BIA-ALCL SCHEER has adapted the text relative to textured implants. It now states:</p> <p>“Based on these data, SCHEER considers that there is a moderate weight of evidence for a causal relationship between textured breast implants and BIA-ALCL, particularly in relation to implants with an intermediate to high surface roughness.</p> <p>At this point it should be noted that i) there are several types of textured implants ii) surface textures of breast implants are not all manufactured in the same way, and iii) implants with diverse surface</p>

			 SCHEER_Comment_by_Dr_Mayo.pdf	<p>textures may also present different benefits. The magnitude of the risk per type of textured implant is difficult to establish due to the low incidence of the risk. Even with macro-textured implants, BIA-ALCL has a very low incidence. Therefore, risk assessments per implant type are needed. Furthermore, the risk should be weighed against the benefits. There is also a need for an unambiguous, clinically validated classification system for breast implants including more parameters than just “surface roughness”.; A history of textured breast implants/expanders appears to be necessary but not sufficient for the development of BIA-ALCL. Another risk factor for BIA-ALCL may arise as a consequence of the manufacturing process for certain types of PU coating.”</p> <p>Based on epidemiology, the text of the conclusion in section 6 was expanded by the addition of this sentence:</p> <p>“As far as the manufacturer for textured implants was known most cases were found for the Biocell implant (textured by salt loss technique), while for PU coated breast implants BIA-ALCL cases were mainly associated with Silimed implant. Cases for other manufacturers were much lower.</p>
81	Cardoso Maria-Joao, Eusoma (European Society of Breast Cancer Specialists), Italy	4.2 Types of breast implants	page 15 line 40 page 16 line 20  scheer_o_018Eusoma comments.pdf	<p>Page 15 line 40. Text on implant choice has been adapted in section 4.1.. Page 15 line 40 indicates possibilities and does not deal with patients choice that is described and discussed in 4.1 as presented below.</p> <p>“Some trends are apparent in the literature for the use of one or another type of breast implant. However, the clinical indications for the use of a specific type of breast implant should depend on a consultation between clinician and patient to allow informed decision making to take place with regards to the choice of an appropriate breast implant. For breast reconstruction a shared consultation with a</p>

				<p>multidisciplinary healthcare team including a pathologist, oncologist, surgeon, breast care nurse, etc should be held with the patient to allow informed decision making to take place with regards to the breast reconstruction procedure as well as the choice of implant. For both aesthetic and reconstructive surgery all aspects of breast implants should be evaluated and discussed with the patient, expressly covering advantages, disadvantages, follow-up procedures and risk factors.”</p> <p>Page 16 line 20. Here a description of possible reconstruction with autologous tissue is described. The choice of treatment and implant is described and discussed in 4.1 as presented above.</p>
82	<p>Mercer Nigel , Plastic, Reconstructive and Aesthetic Expert Advisory Group (PRASEAG), United Kingdom</p>	<p>4.2 Types of breast implants</p>	<p>P14 Line 36: The envelope contains the filling material: this doesn't make sense and is confusing. Consistency is needed in the use of terminology regarding the surface of the implant. The preferable terms are 'shell' or 'outer layer'. It should be made clear that the shell is made of silicone.</p> <p>P14 Line 43: texturing is not referred to as 'mild' or 'heavy'. It is micro or macro. Lay person friendly terminology has not been used anywhere else in this document but, if that is the intention, then Micro (shallow texturing) macro (deep texturing) or smooth (minimal texturing) would be the better.</p> <p>P14 Line 55-56: The surface area in contact does not vary with the number of implants used unless the authors are referring a cumulative total, however there is no evidence presented that cumulative exposure to breast implants increases risk.</p> <p>P14/15: Pictures would be much better for all to understand.</p> <p>P15 Line 11: Lenticular shape: This is not a term used clinically. In the interests of being understood by patients 'dome' shape may be more understandable.</p>	<p>SCHEER agrees with the comment. However, the text clearly described the names for the shell on page 14 in line 36-37. “The shell surface, or outer layer of the implant otherwise known as the envelope, contains the filling material.” The fact that the shell consists of silicone is indicated in the text (line 37).</p> <p>In the text the word “envelope” is replaced by “shell”.</p> <p>P14 line 43. SCHEER agrees and has adapted the text.</p> <p>“The most outer layer represents the surface in contact with patient tissues and can be smooth or rough with different degrees of roughness ranging from macro (with deep texturing), micro (with shallow texturing) to smooth (with minimal texturing).”</p> <p>Page 14 line 55-56. The text does not deal with the total surface area but with the characteristics that can be used to describe the implant surface. These are used here descriptive and not relative to risk.</p> <p>P14/15. A picture of various implant surfaces is present in section 4.6 which discusses implant surface textures.</p>

				P15 line 11. Text changed: “Round implants have a lenticular shape, with a symmetrical curved anterior side (dome) and a flat round posterior base, with no apparent differences in the shape between the top and bottom of the implant.”
83	ATLAN MICHAEL, HEAD OF PLASTIC SURGERY DEPARTMENT HOPITAL TENON APHP PARIS FRANCE, France	4.2 Types of breast implants	Je suis à l'origine de classifications des implants, par la surface area.  Il est important d'unir nos efforts notamment avec les études australiennes afin de faire une classification unifiée.	SCHEER agrees on international cooperation. SCHEER has noted that in ISO context a revision of ISO 14607:2018 is currently started including a revision on the surface characteristics beyond surface roughness.
84	LORETI ANDREA, AZIENDA OSPEDALIERA SAN GIOVANNI ADDOLORATA, ROME - ITALY, Italy	4.3 Alternative s to breast implants	Dear SCHEER members and experts, I would like to congratulate all for your Opinion, and the attention given to women with breast cancer in our countries.  I appreciate your detailed analysis on the state-of-the-art regarding BIA-ALCL, and I would like to comment some points of discussion regarding immediate reconstruction with implants that did not fully meet my expectations.  Clearly, our main and unique purpose is the health of each patient and their quality of life, and we all aim to improve our services.  You state in your Opinion that "the clinical indications for the use of a specific type of breast implant do not depend on the preoperative clinical conditions, but only on the clinician's and patient's preferences, and consequently on industry and/or media information". In addition, you state that "there are several alternatives to breast implants that involve plastic surgery techniques, either using autologous flap tissue or autologous fat transfer".  I would like to express my disagreement with both the above statements, mainly because I always select the type of surgical technique or the type of breast implants according to clinical indications which can vary widely from one patient to another.	Thank you! SCHEER agrees with the comment on choice of implant and has adapted the text on this issue in section 4.1.  ““Some trends are apparent in the literature for the use of one or another type of breast implant. However, the clinical indications for the use of a specific type of breast implant should depend on a consultation between clinician and patient to allow informed decision making to take place with regards to the choice of an appropriate breast implant. For breast reconstruction a shared consultation with a multidisciplinary healthcare team including a pathologist, oncologist, surgeon, breast care nurse, etc should be held with the patient to allow informed decision making to take place with regards to the breast reconstruction procedure as well as the choice of implant. For both aesthetic and reconstructive surgery all aspects of breast implants should be evaluated and discussed with the patient, expressly covering advantages, disadvantages, follow-up procedures and risk factors.”  The text on textured implants has been adapted as well to clarify that not all types of textured implants induce BIA-ALCL.  “Based on these data, SCHEER considers that there is a moderate

		<p>You would certainly agree that every woman with breast cancer undergoing breast reconstruction presents truly unique features, and she is a story for herself. You can find indications for anatomical textured implants, polyurethane implants or, rarely, for reconstruction with autologous tissues.</p> <p>I believe it would be import, therefore, that the Commission takes in serious consideration the strong negative impact that the eventual decision to withdraw textured implants (and consequently anatomical implants) from the market could have on a successful breast reconstruction and therefore on the well-being of women who have already received a devastating diagnosis.</p> <p>Assuming that all patients can be candidates for autologous flap tissue reconstruction (which is not the case), patients need to know that they will undergo extensive surgery sessions, with the possibility of long-term hospitalization.</p> <p>If an alternative to textured implants is the fat transfer, the patient should be aware that the process will be completed in several months if not in years, and that the esthetic result might not be satisfactory.</p> <p>Another point that has not been addressed in this Opinion is the fact that, by discontinuing the use of breast implants, the chances of having a reconstruction following mastectomy would be drastically reduced.</p> <p>In Italy, breast reconstructions with autologous tissues are performed only in major, highly specialized centers. What about breast cancer patients living in small towns, far from big cities? What will happen to women with limited financial resources? Particularly in this pandemic era, it seems to me that limiting implant reconstruction would be deleterious to many thousand of women diagnosed with breast cancer in Europe and necessitating mastectomy.</p> <p>My group at the San Giovanni-Addolorata Breast Center has recently published a clinical paper showing a six-fold lower incidence of severe</p>	<p>weight of evidence for a causal relationship between textured breast implants and BIA-ALCL, particularly in relation to implants with an intermediate to high surface roughness.</p> <p>At this point it should be noted that i) there are several types of textured implants ii) surface textures of breast implants are not all manufactured in the same way, and iii) implants with diverse surface textures may also present different benefits. The magnitude of the risk per type of textured implant is difficult to establish due to the low incidence of the risk. Even with macro-textured implants, BIA-ALCL has a very low incidence. Therefore, risk assessments per implant type are needed. Furthermore, the risk should be weighed against the benefits. There is also a need for an unambiguous, clinically validated classification system for breast implants including more parameters than just “surface roughness”. A history of textured breast implants/expanders appears to be necessary but not sufficient for the development of BIA-ALCL.”</p> <p>Another risk factor for BIA-ALCL may arise as a consequence of the manufacturing process for certain types of PU coating.</p> <p>The fact that multiple procedures may be necessary for AFT is indicated on page 17 line 19-21.</p> <p>SCHEER does not recommend the removal of breast implants from the EU market. SCHEER was mandated to evaluate the risk of breast implants for the occurrence of BIA-ALCL.</p> <p>The need for specific expertise for autologous flap transfer has been addressed on page 16, line 18.</p> <p>“it should be noted that for complicated surgeries for autologous reconstruction involving the various flap transfer techniques, specific expertise and experience is needed that can only be provided in specialised hospitals.”</p>
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			<p>capsular contracture with polyurethane implants especially in case of post-mastectomy radiation therapy.</p> <p>By reading your Opinion, it is clear that there is a great tolerance for round smooth implants. The reason is that it is recognized to smooth implants a risk of BIA-ALCL equal to zero. To the best of my knowledge, current literature does not allow to exclude that BIA-ALCL will ever happen with smooth implants.</p> <p>In conclusion, I firmly advocate you avoid any political decision that could have a catastrophic impact on women in need of breast reconstruction.</p>		<p>The text on textured implants is adapted, so there is no indication that only “smooth” implants should be used for breast reconstruction/augmentation.</p>
85	Sukop Andrej, Czech Society of Plastic Surgery, Czech Republic	4.3 Alternative s to breast implants	<p>Breast implants are commonly used for breast reconstruction in reconstructive plastic surgery and it is not possible to completely substitute them with autologous tissue or adipose tissue transplantation. Breast reconstruction with autologous tissue or adipose tissue transplantation is also associated with numerous possible local and general complications and risks.</p> <p>The use of breast implants in aesthetic surgery aims to achieve a better shape and a larger size of breasts depending on the wish of a patient and in majority of cases, the implants cannot be substituted with adipose tissue transplantation. Very often, adipose tissue transplantation is financially more demanding for the patient, requires several consequent surgeries and also comes with numerous local and general health risks and possible complications.</p>		<p>SCHEER addressed the alternative methods for breast reconstruction/augmentation for completeness and to raise awareness that such alternatives exist. SCHEER does not advocate the use of one method over another.</p>
86	Zic Rado, ESPRAS European Society of Plastic, Reconstructive and Aesthetic Surgery, Croatia	4.3 Alternative s to breast implants	<p>Please see the submitted file</p>  <p>ESPRAS_letter_to_SH EERS_Committee_fin.c</p>		<p>The text on the epidemiology of BIA-ALCL in answer to Q2 has been adapted and now reads as:</p> <p>“The estimation of the lifetime incidence of BIA-ALCL in women with implants has increased as presented in initial reports from 1 per million to current highest overall estimates of approximately 1 per 3000 women in Australia and the Netherlands.”</p> <p>Regarding relation BIA-ALCL with type of implant. The text on textured</p>



			<p>implants has been adapted. However, so far, for almost all (probably with the exception of one) implants of which the surface characteristic was known, it was identified as textured.</p> <p>““Based on these data, SCHEER considers that there is a moderate weight of evidence for a causal relationship between textured breast implants and BIA-ALCL, particularly in relation to implants with an intermediate to high surface roughness.</p> <p>At this point it should be noted that i) there are several types of textured implants ii) surface textures of breast implants are not all manufactured in the same way, and iii) implants with diverse surface textures may also present different benefits. The magnitude of the risk per type of textured implant is difficult to establish due to the low incidence of the risk. Even with macro-textured implants, BIA-ALCL has a very low incidence. Therefore, risk assessments per implant type are needed. Furthermore, the risk should be weighed against the benefits. There is also a need for an unambiguous, clinically validated classification system for breast implants including more parameters than just “surface roughness”. A history of textured breast implants/expanders appears to be necessary but not sufficient for the development of BIA-ALCL. Another risk factor for BIA-ALCL may arise as a consequence of the manufacturing process for certain types of PU coating.”</p> <p>Regarding implant choice. Text has been adapted:</p> <p>““Some trends are apparent in the literature for the use of one or another type of breast implant. However, the clinical indications for the use of a specific type of breast implant should depend on a consultation between clinician and patient to allow informed decision making to take place with regards to the choice of an appropriate</p>
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				breast implant. For breast reconstruction a shared consultation with a multidisciplinary healthcare team including a pathologist, oncologist, surgeon, breast care nurse, etc should be held with the patient to allow informed decision making to take place with regards to the breast reconstruction procedure as well as the choice of implant. For both aesthetic and reconstructive surgery all aspects of breast implants should be evaluated and discussed with the patient, expressly covering advantages, disadvantages, follow-up procedures and risk factors.”
87	Parreira Carlos, EASAPS ESAPS, Belgium	4.3 Alternatives to breast implants	<p>4.3. Alternatives to breast implants  “Breast implants are used in aesthetic procedures for the correction of developmental anomalies of the breast such as amastia, hypoplasia, breast asymmetry, tuberous breast and when breast volume augmentation is desired. AFT, as in breast reconstruction, is an autologous alternative to breast implants, offering comparable results. However, AFT often requires more surgical procedures, as described above.”</p> <p>Line 23 4.3d Alternatives in aesthetic cases presents 5 lines on aesthetic emphasizing rare aesthetic indications and suggesting fat transfer as option which is totally unacceptable and this paragraph should be vastly extended outlining the negative consequences and lack of quality alternatives. The SCHEER report states that, for aesthetic purposes, fat grafts offer comparable results to breast implants but do not refer to the unpredictability and other issues of fat transfer.</p> <p>Please change to:  “Breast implants are used in aesthetic procedures for the correction of developmental anomalies of the breast such as amastia, hypoplasia, breast asymmetry, tuberous breast and when breast volume augmentation is desired. Fat grafting procedures are widely employed in aesthetic and reconstructive surgery. It should however be stated that the predictability of outcomes with autologous fat transfer still is questionable. Patients have to undergo several operative sessions for</p>	<p>SCHEER disagrees. The Opinion is evaluating the risk of breast implants in relation to BIA-ALCL. Alternatives for breast implants are presented, but this Opinion does not aim to provide an extensive overview of all possible alternatives for breast implants.</p> <p>SCHEER agrees with the comment on the multiple procedures needed and the uncertainty of the final result.</p> <p>Text adapted:  “Breast implants are used in aesthetic procedures for the correction of developmental anomalies of the breast such as amastia, hypoplasia, breast asymmetry, tuberous breast and when breast volume augmentation is desired. AFT, as in breast reconstruction, is an autologous alternative to breast implants, offering comparable results. However the predictability of outcomes with autologous fat transfer may be uncertain, especially in cases in which radiotherapy was applied. Also patients have to undergo several operative sessions for aesthetic purposes. Moreover, repetitive fat graft sessions might not be possible in some patients because of unavailability of the required fat volume (e.g. low Body Mass Index).”</p>

			aesthetic purposes even without taking into account that preoperative effects of irradiation therapy in some patients make take-rates of fat grafts even more unpredictable. Moreover, repetitive fat graft sessions might not be possible in some patients because of unavailability of the required fat volume (low BMI). The aspect of long-term oncologic safety of fat grafts still remains to be fully investigated. “	
88	Cristian Radu Jecan, Romanian Association of Plastic Surgeons, Romania	4.3 Alternatives to breast implants	page 15 - lines 25 - 29. RoAPS supports E(A)SAPS comments - The SCHEER report states that, for aesthetic purposes, fat grafts offer comparable results to breast implants but do not refer to the unpredictability and other issues of fat transfer. Fat grafting procedures are widely employed in aesthetic and reconstructive surgery. It should however be stated that the predictability of outcomes with autologous fat transfer still is questionable. Patients have to undergo several operative sessions for aesthetic purposes even without taking into account that preoperative effects of irradiation therapy in some patients make take-rates of fat grafts even more unpredictable. Moreover, repetitive fat graft sessions might not be possible in some patients because of unavailability of the required fat volume. The aspect of long-term oncologic safety of fat grafts still remains to be fully investigated. E(A)SAPS would like to put emphasis on these statements since autologous tissue transfers are seldomly indicated in aesthetic conditions aside from some patients after massive weight loss or congenital malformations. E(A)SAPS agrees that described alternatives are important to consider for reconstructive indications, but SCHEER puts insufficient emphasis on these aspects of alternatives for aesthetic patients who represent 70-80% of indications for breast enlargements.	Text on autologous fat transfer has been adapted, and now indicates uncertainty of outcomes:  “Breast implants are used in aesthetic procedures for the correction of developmental anomalies of the breast such as amastia, hypoplasia, breast asymmetry, tuberous breast and when breast volume augmentation is desired. AFT, as in breast reconstruction, is an autologous alternative to breast implants, offering comparable results. However the predictability of outcomes with autologous fat transfer may be uncertain, especially in cases in which radiotherapy was applied. Also patients have to undergo several operative sessions for aesthetic purposes. Moreover, repetitive fat graft sessions might not be possible in some patients because of unavailability of the required fat volume (e.g. low Body Mass Index).”
89	Mercer Nigel, Plastic, Reconstructive and Aesthetic Expert Advisory Group (PRASEAG), United Kingdom	4.3 Alternatives to breast implants	P15 Line 42: Alternatives to breast implants following breast conserving techniques: This does not read well and is too long. Implants are not used after Breast Conserving Surgery, because of the need for radiotherapy. Is the message here to avoid mastectomy and, therefore, reconstruction by using oncoplastic surgery techniques.  P15 Line 51: For larger resections, the feasibility of therapeutic mammoplasty is entirely dependent on the patient’s breast size. The need for radiotherapy after breast conserving surgery must be mentioned. Radiotherapy carries morbidity (long term mild chronic pain	P15 line 42. The intention is to sum up possible alternatives for breast implants. Not to indicate a preference for one or the other.  P15 line 51. Text added on radiation therapy. P15 line 55.  “However, it should be noted that the need for radiotherapy any type of surgery may hamper tissue healing/regeneration.”  P16 line 2. Text on limitations have been added.

			<p>is common, as well as firmness and atrophy) and a risk of angiosarcoma.</p> <p>P16 Line 2: The implication is that these other techniques are suitable to all patients is simply incorrect. They don't work in slim patients devoid of skin redundancy.</p> <p>P16 Line 5-41: Alternatives to breast implants following mastectomy: This seems over detailed for the purposes of this report.</p> <p>P16 Line 5-21: Autologous fat transfer: This is not really an option for breast reconstruction at present and not really a substitute for implants at present.</p> <p>P16 Line 23: Alternative to implants for aesthetic breast surgery: It should be stated there are very few alternatives (other than fat transfer for small volume augmentation) and give a better explanation why reconstructive procedure are less appropriate for aesthetic surgery.</p>	<p>"Patients characteristics (e.g. a slim body with a low Body Mass Index) can limit the use of such techniques."</p> <p>P16 line 5-41. SCHEER agrees and has deleted part of the text discussing the various flap types. P16 line 22-and P17 line 4 have been deleted.</p> <p>Text modified: "Tissue flap selection is based on donor site availability and the surgeon's experience. It should be noted that for complex surgeries for autologous reconstruction involving the various flap transfer techniques, specific training, expertise and experience as is usually present in specialised hospitals."</p> <p>P16 line 5-21. SCHEER disagrees. It is an option even when specific requirements must be fulfilled to perform AFT.</p> <p>P16 line 23. According to SCHEER, due to the very limited indication it does not seem appropriate to discuss procedures for reconstructive surgery to be used for aesthetic purposes. In addition, reconstructive surgery is accompanied with a more complex surgery (in case of flap augmentation) in patients in which this is not necessary when less invasive procedures are available.</p>
90	CAMPANALE ANTONELLA, ITALIAN MINISTRY OF HEALTH, Italy	4.3 Alternative s to breast implants	<p>p. 15 line 33-40: This sentence confirms that clinical indication for the use of one type of breast implant versus another, as well as surgical procedures, DEPENDS on the preoperative clinical condition. This sentence is in contradiction with the sentence reported in the paragraph 2.1 ANSWERS TO THE TERMS OF REFERENCES page 9 line 17-20</p> <p>p. 16 line 5:Autologous reconstruction techniques requires a great surgical expertise and physicians are not always able to perform it as reported even by the WG at paragraph 4.3 ALTERNATIVES TO BREAST IMPLANTS page 16 line 20: "Flap selection is based on donor site availability and the surgeon's experience". There is the high risk that many patients do not receive reconstruction.</p> <p>p. 16 line 27-28: Pedicle flaps like the Latissimus Dorsi flap (LD) are</p>	<p>P15 line 33-40. Text adapted:  ""The choice of technique is decided in a shared decision-making process between clinicians and patients taking into consideration several aspects including preoperative clinical conditions.""</p> <p>P16 line 5. SCHEER agrees and therefore has included the statement on donor site availability AND surgeon's experience.</p> <p>Text added:  "Tissue flap selection is based on donor site availability and the surgeon's experience. It should be noted that for complex surgeries for autologous reconstruction involving the various flap transfer techniques, specific training, expertise and experience as is usually present in specialised hospitals."</p> <p>P16 line 27-28. As an extensive discussion on various flap techniques</p>

		<p>frequently used for breast reconstruction, but the WG omits to report that it is mostly used with an anatomical breast implant to restore shape and volume (following references), and the use of the flaps from the thoracodorsal donor area increases the operative morbidity and is contraindicated for patients with ASA index III-IV. AFT can be used to improve volume but is not always possible as it depends on the amount of fat tissue available for multiple surgical sessions. Therefore, total reconstruction with LD plus AFT (without an implant) is indicated only in few patients with available fat tissue. Latissimus dorsi muscle flap and tissue expansion for breast reconstruction. Mimoun M, Chaouat M, Lalanne B, et al. <i>Ann Plast Surg.</i> 2006;57:597–601; Patient-reported outcomes and their predictors at 2- and 3-year follow-up after immediate latissimus dorsi breast reconstruction and adjuvant treatment. Winters ZE, Afzal M, Balta V, et al. <i>Br J Surg.</i> 2016;103:524–536; Immediate breast reconstruction with latissimus dorsi flap and implant: audit of outcomes and patient satisfaction survey. Venus MR, Prinsloo DJ. <i>J Plast Reconstr Aesthet Surg.</i> 2010;63:101–105.</p> <p>p.17 line 7-8: This alternative is indicated for a specific type of mastectomy (i.e. nipple-sparing mastectomy, like the same sentence states) and the reconstructive procedure is rarely used FOR TOTAL BREAST RECONSTRUCTION because it depends on the amount of fat tissue available and transferred by multiple surgical sessions, as the same WG states at pag 17 line 14 “Usually, to form a proper connection, the amount of fat needed to restore the required breast volume cannot be transferred in a single procedure, instead requiring more surgical procedures”</p> <p>p.17 line 27-28: Although AFT has been shown to excel in the restoration of contour deformities, it cannot be proposed as an alternative to breast implant augmentation because it depends on the amount of fat tissue available for multiple surgical sessions. Moreover, regarding the comparable results, the WG should add references to support this statement. Finally, AFT is a procedure with unpredictable rate of fat taking, complications and unstable long-term results (please look at the following paper: Kang D, Luan J. Fat Necrosis After Autologous Fat Transfer (AFT) to Breast: Comparison of Low-Speed</p>	<p>is outside the scope of the Opinion the text on flap techniques has been shortened, just indicating the possibilities. The combination of AFT and surgical (flap) techniques has been indicated on page 17 line 7-10.</p> <p>P17 line 7-8 The reference to the specific procedure (nipple sparing mastectomy) is removed to indicate a more wider possible application of the technique.</p> <p>Text and reference added.  “The advantage of AFT over flap surgery is that it produces fewer scars, however, like all surgical procedures there is a risk for complications (Kontoes and Gounnaris 2017, Kang and Luan 2018).</p>
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			Centrifugation with Sedimentation. Aesthetic Plast Surg. 2018 Dec;42(6):1457-1464)	
91	BENITO-RUIZ JESUS, ANTIAGING GROUP BARCELONA, Spain	4.3 Alternative s to breast implants	lines 27-28  AFT does not provide comparable results to implants. The volume to be used is much less (it depends on the recipient site capacity), there is variable degree of resorption and the graft does not project. It needs extensive surgery (liposuction) with risks associated to this procedure. Results can be comparable to AFT in reconstructive settings, but not with implants. This is why composite breast augmentation (fat grafting plus breast implants) are the gold standard now	Text adapted:  “The advantage of AFT over flap surgery is that it produces fewer scars, however, like all surgical procedures there is a risk for complications (Kontoes and Gounnaris 2017, Kang and Luan 2018).”
92	atlan Michael, APHP PLASTIC SURGERY DEPARTMENT TENON APHP PARIS, France	4.3 Alternative s to breast implants	I do not think fat grafting and autologous Free flaps, are not alternatives to breast implants at all. The 3 are options for patients and often are used together .  As example , as a reconstructive breast surgeon, it's very often that i mix autologous flap and fat grafting because the outcome is not perfect, and the same for implants/  AUtologous flap are not comparable to breast implants ; you need adipose reserve and excess (lower belly , inner thigh or gluteal regions) and not every women are the same !!! If you ban breast implants thin women will be enable to be reconstructed !  Even autologous flap are very good and beautiful reconstruction : soft and hot breast (not the case for every implant based reconstruction), no need for implant exchange because of ruptured implants or capsular contracture.... , theses techniques of free flaps need: special skills in microsurgery (i practice 2 cases per week) which are not so spread , free flap are time consuming surgery- long surgery 3-4 hours in trained teams,... and you need additional scars on the body !!!! and not short for a diep flap the more used flap the scar is low on the belly but could measures 50 cm long in addition with the mastectomy scar. With implants you dont need additional scars!  Fat grafting is very useful for breast reconstruction after cancer and	SCHEER acknowledges the comment. The intention is to sum up possible alternatives for breast implants, not to indicate a preference for one or the other. The final choice should be based on the consultation between surgeon and patient. As indicated in section 4.3 page 15 line 33-34 which states:  “The choice of technique is decided in a shared decision-making process between clinicians and patients taking into consideration several aspects, including preoperative clinical conditions:”

			<p>malformation but is often not enough alone to get a good outcome .Indeed fat grafting has a resorption rate of 40% minimum and we need enough fat has to harvest be present if you want to reconstruct a whole breast. Again , thin or not overweighted women are not very good candidate Its very rare that this technique will be enough to build a medium size breast ...and need 2-5 or 6 sessions under general anesthesia especially after irradiation. Fat grafting is more often used as ancillary procedure , in addition with free flaps and breast implants</p> <p>So .... There is many techniques for very different patients FAT GRAFTING AND FREE AUTOLOGOUS FLAP are not ALTERNATIVES but different treatments for different patients. the ban on breast implants will eliminate a very useful and important type of reconstruction and will exclude many patients from breast recon after breast cancer or breast malformation!</p>	
93	Mureau Marc, Erasmus MC Cancer Institute, University Medical Center Rotterdam, the Netherlands, Netherlands	4.3 Alternative s to breast implants	<p>I miss the differences in complication risks and types between implant breast reconstruction and autologous breast reconstruction. In addition, it should be clear that virtually all autologous techniques are far more invasive than implant surgery and lead to additional donor-site scarring and possibly complications. Also, not all women are candidates for these alternative techniques because of co-morbidity, lack of donor-site tissues, or because of patient preferences (in case the patient does not want such an invasive procedure). In conclusion, there are many women for whom there are no reasonable alternatives to breast implants, contrarily to popular/public belief.</p> <p>This is all the more true for aesthetic breast enlargements. For the AFT paragraph, I would suggest to include the additional use of the BRAVA system which oftentimes seems necessary to improve the results of lipofilling.</p>	<p>SCHEER acknowledges the comment. The intention is to sum up possible alternatives for breast implants, not to indicate a preference for one or the other. The final choice should be based on the consultation between surgeon and patient. As indicated in section 4.3 page 15 line 33-34 which states:</p> <p>“The choice of technique is decided in a shared decision-making process between clinicians and patients taking into consideration several aspects, including preoperative clinical conditions:”</p> <p>Text adapted to include the non surgical tissue expansion. “Fat transfer can be combined with a non surgical tissue expansion by sustained tension (generated by a low negative pressure) on the natural breast tissue to cause the cells to expand and replicate (Oranges et al., 2018). “</p>
94	Parreira Carlos, EASAPS ESAPS,	4.4 Breast Implant	“Concerns of a possible association between breast implants and ALCL first arose in the mid-1990s (Duvic et al., 1995; Keech and Creech, 1997)	SCHEER agrees that it is too premature to indicate texture here. Text has been adapted.

	Belgium	Associated - Anaplastic Large Cell Lymphoma	<p>and have now become a serious issue with respect to the use of textured breast implants.”</p> <p>This is serious, full stop. Texturization is under investigation and needs to be further monitored as all other aspects of the implant shell not only texturization. Replace with: “Concerns of a possible association between breast implants and ALCL first arose in the mid-1990s (Duvic et al., 1995; Keech and Creech, 1997) and have now become a serious issue.”</p> <p>If you want to insist on textured: “Concerns of a possible association between breast implants and ALCL first arose in the mid-1990s (Duvic et al., 1995; Keech and Creech, 1997) and have now become a serious issue with respect to the use of Biocell textured breast implants.”</p>	Text adapted. Deleted “of textured implants” .
95	Mercer Nigel, Plastic, Reconstructive and Aesthetic Expert Advisory Group (PRASEAG), United Kingdom	4.4 Breast Implant Associated - Anaplastic Large Cell Lymphoma	<p>P18 section 4.4.2: The addition of subheadings would make this section more readable.</p> <p>P18 Line 33: The ‘exceptional case’ occurring earlier than one year was in a patient who had implant exchange and the ALCL occurred less than one year after that procedure. In the knowledge that there have been late cases in residual capsules, is it scientifically appropriate to stay the BIA-ALCL was causally linked with the second implant. Have there been any BIA-ALCL cases so soon after single implant usage?</p> <p>P18 Line 46: ALL of the seroma fluid should be aspirated and analysed. Mention of the difficulty of diagnosis and false negative aspiration is required.</p> <p>P19 Line 2: ‘considerable symptomatic fluid accumulation’: ‘Fluid accumulation sufficient to cause a visible difference in breast size’ would be better.</p> <p>P19 Line 20: BIA-ALCL is considered to be related to the use of the device: Use of ‘Implant’ for ‘device’ would make understanding by the lay person easier.</p>	<p>P18 section 4.4.2. a number of headings has been introduced.</p> <p>P18 line 33. Which implant is causative is not really known The latest implant is used as a starting point. When possible the history of implants is further evaluated, but this is not always clear/possible.</p> <p>P18line 46. Only a minimum is indicated for a proper diagnosis. Removal of all seroma can be part of the therapy.</p> <p>Text added. “BIA-ALCL diagnosis based on the seroma aspirate may be difficult.”</p> <p>P19 line2. SCHEER agrees. Text adapted: “While a small amount of fluid (10-15 mL) can be normal around most breast implants, a considerable symptomatic fluid accumulation, for example sufficient to cause a visible difference in breast size should also be investigated by cytological evaluation for the presence of BIA-ALCL (Chacko and Lloyd, 2018).” P19 line 20 SCHEER agrees. “device” replaced by “implant”.</p>




			P20. Table 2: What are columns 2 and 3 saying? This needs better explanation. Column 6 better phrased 'Guidelines for early diagnosis'	P20 Table 2. The headings of Table 2 are recommendations from governments. Government do not publish "guidelines" for plastic surgery or pathological diagnosis. Guidelines are established by scientific communities.
96	Decaluwé Kelly, The Federal Agency of Medicines and Health Products , Belgium	4.4 Breast Implant Associated - Anaplastic Large Cell Lymphoma	Page 17, line 33 - 35 BIA-ALCL has become a serious issue with respect to the use of breast implants in general. The role for smooth implants is at this stage not yet fully excluded and therefore awareness must be maintained for all types of breast implants and not only for textured breast implants. The FAMHP would suggest to slightly alter the sentence accordingly: ' ... and have now become a serious issue with respect to the use of breast implants and especially breast implants with a textured surface.'	Text adapted. Deleted "of textured implants".
97	CAMPANALE ANTONELLA, ITALIAN MINISTRY OF HEALTH, Italy	4.4 Breast Implant Associated - Anaplastic Large Cell Lymphoma	p. 17 line 33-35: We believe that, to date, any type of breast implants (both smooth and textured) should be monitored without any preconceptions and anyway until the exclusion of smooth devices in the pathogenesis of this disease will be proved. Therefore we propose to modify this sentence as following: "Concerns of a possible association between breast implants and ALCL first arose in the mid-1990s (Duvic et al., 1995; Keech and Creech, 1997) and have now become a serious issue with respect to the use of breast implants".	SCHEER agrees. Text adapted. Deleted "of textured implants".
98	No agreement to disclose personal data	4.4.2. Breast Implant Associated - Anaplastic Large Cell Lymphoma (BIA-ALCL)	Page 20, table Health Products Regulatory Association is incorrect.  The correct name is 'Health Products Regulatory Authority'.	SCHEER agrees. Name adapted to the one provided.
99	AYHAN SUHAN, GAZI UNIVERSITY FACULTY OF MEDICINE, TURKEY	4.4.2. Breast Implant Associated - Anaplastic	First of all, BIA-ALCL is a rare disease with a stable increase. There are approximately 1000 diagnosed cases worldwide since the first case described in 1997. However, it has been estimated that more than 20 million implants were sold all around the world only in the last 10 years. The number of cases increased after 2007, especially after the Allergan Biocell implants were popularized. Eventually, Allergan Biocell implants	SCHEER agrees with the comment. This is addressed in section 6.2

		Large Cell Lymphoma (BIA-ALCL)	were found to be responsible in more than 85% of the cases and thus the company has stopped producing these implants and called back the products all over the world. In rest of the cases, implants of other manufacturers, such as Mentor, Silimed, Nagor, PIP and Polytech are associated in a decreasing order 1 . According to the latest update of the FDA in January 20202, textured implants constitute 68%, smooth implants constitute 4% of the cases, where in 28% of the cases the surface of the implants are still not specified.	
100	Cardoso Maria-Joao, Eusoma (European Society of Breast Cancer Specialists), Italy	4.4.2. Breast Implant Associated – Anaplastic Large Cell Lymphoma (BIA-ALCL)	page18 lines 22-23  scheer_o_018Eusoma comments.pdf	Headings are now included in section 4.4.2.
101	Decaluwé Kelly, The Federal Agency for Medicines and Health Products , Belgium	4.4.2. Breast Implant Associated – Anaplastic Large Cell Lymphoma (BIA-ALCL)	Page 20, table 2 We believe this table does not correctly reflects the situation in Belgium. The article that published this table did not provide the source of the information. It could be that the author(s) do(es) not fully comprehend the specifics of Belgian law, Belgian state structure and the division of competences between public administrations. Belgium has several ministers who have a competence in Public Health of which 1 federal minister and multiple regional ministers.  For breast implants the most important one would be the Federal Minister who is responsible for Public Health. The Federal Public Service (FPS) Health, Food Chain Safety and Environment has many responsibilities in the field of public health (shared with the regional public services) but the medical devices including breast implants is not one of them. That is a competence of the Federal Agency for Medicines and Health Products. The FAMHP reports directly to the Federal health Minister.  According to our Royal Decree for medical devices of March 18, 1999	Table 2 has been adapted according to the comment.

			<p>there is a national obligation by law for health care professionals to report all incidents with medical devices to the FAMHP. This obligation includes reporting of BIA-ALCL cases. As such the "report mandatory" field should state "YES".</p> <p>On the other hand there are no specific recommendations issued by the FAMHP for the use of implants with a certain type of texture. As such the "recommendation towards all textured implants" field should be "NO".</p> <p>The FAMHP has together with the Superior Health Council (which is the scientific advice board of the Federal Public Service (FPS) Health, Food Chain Safety and Environment) written a publication on BIA-ALCL:(<a href="https://www.health.belgium.be/sites/default/files/uploads/fields/fpshealth_theme_file/shc_9473_bia_alcl.pdf">https://www.health.belgium.be/sites/default/files/uploads/fields/fpshealth_theme_file/shc_9473_bia_alcl.pdf</a>).</p> <p>The FAMHP has thus issued health recommendations and recommendations for early diagnosis. As such the field "Ministry of Health recommendations" and the "Recommendatons for early diagnosis should both state "YES".</p> <p>In summary, to accurately reflect the Belgian situation the table should be adapted as following: YES, NO, YES, YES.</p> <p>The FAMHP also advises to consult the other regulatory boards in order to verify whether the data for all EU countries provided within this report is accurate.</p>	
102	Decaluwé Kelly, The Federal Agency of Medicines and Health Products , Belgium	4.4.2. Breast Implant Associated – Anaplastic Large Cell Lymphoma (BIA-ALCL)	<p>Page 18, line 40 - 41</p> <p>Proper early diagnosis plays an important role with respect to disease prognosis. It might therefore be opportune to provide a little more detail on the use and relevance of each of these imaging techniques. Ultrasound is indeed the first choice to determine fluid accumulation within the breast but MRI could be helpful in those cases for which ultrasound examination is undetermined. Also the role of the PET-CT scan being the identification of metastatic lesions in confirmed cases is not specified within the report.</p>	<p>This Opinion does not intend to provide an exhaustive description of all diagnostic tools available for diagnosis of BIA-ALCL. Text has been adapted to include PET-CT as an additional diagnostic technique.</p> <p>” Breast scanning techniques that can be used for BIA-ALCL diagnosis include computed tomography (CT), positron emission tomography (PET), PET-CT combined and magnetic resonance imaging (MRI).”</p>

103	Decaluwé Kelly, The Federal Agency of Medicines and Health Products, Belgium	4.4.2. Breast Implant Associated – Anaplastic Large Cell Lymphoma (BIA-ALCL)	Page 18, line 25 In this section the word 'uncommon' has been used to indicate the frequency of occurrence of BIA-ALCL. On page 35, line 49 for example the authors use the word 'rare'. Since these terms are no synonyms, the FAMHP would suggest to use the same term throughout the text when indicating frequency of occurrence of the disease.	SCHEER agrees. The word “uncommon” is now used throughout the Opinion.
104	CAMPANALE ANTONELLA, ITALIAN MINISTRY OF HEALTH, Italy	4.4.2. Breast Implant Associated – Anaplastic Large Cell Lymphoma (BIA-ALCL)	<p>p. 18 line 25- 30:Please note that although some references have been mentioned, our studies have not been considered. Please add and comment the reference Campanale 2020 after the first sentence: “....Generally, BIA-ALCL follows an indolent clinical course and has an excellent prognosis when diagnosed and treated promptly (Campanale 2020)....”</p> <p>p. 19 line 26-28:Please add and comment our references (Campanale 2018 (a) and Campanale 2020) in which emerge that Italy produced recommendations for early diagnosis and has established a mandatory notification of each case to the IMoH, centralizing the collection of data.</p> <p>p. 20 line 5- 14:Please add and comment our references (Campanale, 2020)</p> <p>p.20 line 14-15: In order to give to the reader an unbiased message, as the increasing rate of diagnoses is due to the improved awareness on BIA-ALCL issue as well, we believe that the sentence should be completed as the following: “Thanks to the increased awareness on the BIA-ALCL issue, the rate of diagnosis of BIA-ALCL has risen considerably over the 15 past few years.”</p> <p>References: Campanale 2020: The Crucial Role of Surgical Treatment in BIA-ALCL Prognosis in Early- and Advanced-Stage Patients. <i>Plast Reconstr Surg.</i> 2020 Nov;146(5):530e-538e. Campanale 2018 (a): 22 Cases of Breast Implant-Associated ALCL: Awareness and Outcome Tracking from the Italian Ministry of Health.</p>	<p>P18line 25-30. Text adapted.</p> <p>“Generally, BIA-ALCL follows an indolent clinical course and has an excellent prognosis when diagnosed and treated promptly (Campanale et al. 2020).”</p> <p>P19 line26-28. The text already includes the statement on recommendations for diagnosis, and information on Italy was already included in Table 2.</p> <p>P20line5-14. This text deals with the association/relationship between breast implants and BIA-ALCL not with treatment or early diagnosis as described in Campanale et al 2020.</p> <p>P20line14-15. This has been addressed in SECTION 2 Conclusions and in the answer to Q3. Text added:</p> <p>“. In addition, the increase in awareness on the occurrence of BIA-ALCL also contributes to a rise in the rate of BIA-ALCL diagnosis.”</p>

			Plast Reconstr Surg. 2018 Jan;141(1):11e-19e.	
105	Mureau Marc, Erasmus MC Cancer Institute, University Medical Center Rotterdam, the Netherlands, Netherlands	4.4.2. Breast Implant Associated – Anaplastic Large Cell Lymphoma (BIA-ALCL)	In Table 2, I the Netherlands is lacking. In the Netherlands, we do have recommendations regarding the use of textured breast implants. Please add the following data. Country: NL Regulatory Board: Health and Youth Care Inspectorate Report mandatory: YES Recommendation towards all textured implants: YES Ministry of Health Recommendations: YES Recommendations for early diagnosis: YES	NL added to Table 2.
106	Cardoso Maria- Joao, Eusoma (European Society of Breast Cancer Specialists), Italy	4.5 Treatment and prognosis of Breast Implant Associated - Anaplastic Large Cell Lymphoma	page 21 lines 18;29  scheer_o_018Eusoma comments.pdf	Text on spontaneous regression has been added including references.  Text in 4.5 modified:  “Based on the epidemiology, it was suggested that the uncommon occurrence of BIA-ALCL might be a consequence of spontaneous regression/resolution of the disease (Fleming et al., 2018, 2020, 2020). To date true cases of spontaneous regression/resolution of BIA-ALCL have not been reported. Of note, cases described by Fleming et al. as spontaneously regressing were treated, and only reduced numbers of BIA-ALCL cell numbers were observed rather than a complete absence. In general, BIA-ALCL has a favourable prognosis (Clemens et al. 2016, 2018).”  Fleming D, Stone J, Tansley P. Spontaneous Regression and Resolution of Breast Implant-Associated Anaplastic Large Cell Lymphoma: Implications for Research, Diagnosis and Clinical Management. Aesthetic Plast Surg. 2018 Jun;42(3):672-678. doi: 10.1007/s00266-017-1064-z. Epub 2018 Feb 14.  Fleming D, Stone J, Tansley P. Spontaneous Regression and Resolution of Breast Implant-Associated Anaplastic Large Cell Lymphoma: Implications for Research, Diagnosis and Clinical Management.


				<p>Aesthetic Plast Surg. 2020 Aug;44(4):1109-1115. doi: 10.1007/s00266-020-01810-2. Epub 2020 Aug 5.</p> <p>Fleming D, Stone J, Tansley P. Update: Spontaneous Regression and Resolution of Breast Implant-Associated Anaplastic Large Cell Lymphoma—Implications for Research, Diagnosis and Clinical Management—Our Reflections and Current Thoughts Two Years On. Aesth Plast Surg (2020) 44:1116–1119</p>
107	<p>Mercer Nigel, Plastic, Reconstructive and Aesthetic Expert Advisory Group (PRASEAG), United Kingdom</p>	<p>4.5 Treatment and prognosis of Breast Implant Associated - Anaplastic Large Cell Lymphoma</p>	<p>P21: There is hardly any detail about the surgery yet a lot of detail about chemotherapy, that is rarely needed. Better balance is required when describing the treatments. Surgery should be explained in more detail or an appropriate linked reference provided. This should include what a total capsulectomy involves, including how this varies with implant placement, and its potential complications, including pneumothorax. This is important because it is a reason why we do not recommend preventative explanation.</p> <p>P21 Line 31-34: The preferred staging is TNM not the Ann Arbour lymphoma staging and use of the term stage II should be accompanied by text specifying the stages.</p> <p>P21 Line 38-43: This does not reflect modern axillary staging principles. The breast drains to multiple nodal basin but over 75% is towards the axilla and it is likely there will be a similar drainage pattern for the implant capsule/BIA-ALCL. Pre-surgery diagnostic/staging imaging such as US, MRI or PET-CT should help to determine the clinical axillary stage. Any axillary nodes suspicious on standard criteria MUST undergo biopsy with FNA or core biopsy prior to surgery and a positive node would require axillary clearance. The role of SLNB for a clinically negative axilla is unknown in BIA-ALCL but is not precluded if there is clinical uncertainty or suspicion.</p> <p>P21 Line 45: Patients do not fail surgical therapy. Surgery may fail patients! This is now unacceptable terminology. Better phrasing would be, 'if systemic therapy is required'.</p>	<p>P21. SCHEER disagrees. Only limited information is provided on chemotherapy. The Opinion presents a brief overview of therapy possibilities. It is not intended to provide an extensive overview. Any treatment is based on a choice between clinician and patient.</p> <p>P21line 31-34. Text adapted. Paragraph has been deleted and text moved to P21 lines 17-19.</p> <p>P21line38-43. Text adapted to indicate importance of axillary lymph nodes. “Because an implant capsule can drain to multiple regional lymph node basins, even when most of the breast drains to the axillary lymph nodes, there appears to be no role for sentinel lymph node biopsy.”</p> <p>Text indicates further investigation of axillary (and any other) lymph nodes after clinical examination or positive imaging.</p> <p>P21line45. Text adapted. “For patients with proven disseminated disease or patients in which surgical therapy alone fails, oncologists may consider a systemic chemotherapy regimen . . . .”</p> <p>P21line54-55. Text adapted:</p>

			<p>P21 Line 54-55 This section needs to be re-phrased. ‘After surgery for BIA-ALCL, immediate or delayed breast reconstruction or further augmentation has been reported using smooth implants or autologous techniques. The patient needs to be fully informed regarding current uncertainty about the safety of ‘smooth’ implants with regards to BIA-ALCL and capsule formation.</p>	<p>“After surgery for BIA-ALCL, immediate or delayed breast reconstruction or further augmentation has been reported using breast implants or autologous tissue (Lamaris et al. 2019). The patient needs to be fully informed regarding current uncertainty about the safety of various types of breast implants with regards to BIA-ALCL and capsule formation.”</p>
108	CAMPANALE ANTONELLA, ITALIAN MINISTRY OF HEALTH, Italy	4.5 Treatment and prognosis of Breast Implant Associated - Anaplastic Large Cell Lymphoma	<p>p. 21 line 5-15: Note that also in this case, no references to the work and actions undertaken by the IMoH have been made. Please add and comment the following references:</p> <p>The Crucial Role of Surgical Treatment in BIA-ALCL Prognosis in Early- and Advanced-Stage Patients. Campanale A, Spagnoli A, Lispi L, Boldrini R, Marletta M. <i>Plast Reconstr Surg.</i> 2020 Nov;146(5):530e-538e. Online first since August 2020</p> <p>22 Cases of Breast Implant-Associated ALCL: Awareness and Outcome Tracking from the Italian Ministry of Health. Campanale A, Boldrini R, Marletta M. <i>Plast Reconstr Surg.</i> 2018 Jan;141(1):11e-19e.</p>	<p>P21line 5-15. The Opinion on Page21 line5-15 indicates the publication of guidelines for BIA-ALCL. Although the importance of guidelines is mentioned in the papers indicated in the comment by Campanale et al., they do not contain guidelines themselves. Both papers emphasize the importance of registries that is addressed elsewhere in the Opinion.</p>

		<p>In both of them we referred to the importance to follow specific guidelines for the diagnosis, management and treatment of the BIA - ALCL affected patients and the importance of a multidisciplinary approach.</p> <p>p.21 line 17: Please add and comment the following reference: Crucial Role of Surgical Treatment in BIA-ALCL Prognosis in Early- and Advanced-Stage Patients. Campanale A, Spagnoli A, Lispi L, Boldrini R, Marletta M. <i>Plast Reconstr Surg.</i> 2020 Nov;146(5):530e-538e.</p> <p>p. 21 line 27-29: We agree with this prophylactic approach but we believe that this important message for the reader is in contradiction with the sentence reported at page 21 line 54-55: “Physicians can consider immediate or delayed reconstruction with smooth implants or autologous reconstruction based on the stage of disease (Lamaris et al., 2019)”.</p> <p>p. 21 line 54-55: We believe that, with the improved knowledge on the BIA-ALCL issue, in order to give a correct message for the reader, this sentence should be modified as the following: “Although some physicians can consider immediate reconstruction with smooth implants (Lamaris et al., 2019), the NCCN guidelines recommend removal of the contralateral uninvolved implant and capsule to avoid the risk of contralateral disease, which presents in up to 4.6% of patients”. In this way this sentence is coherent with the previous sentence at page 21 line 27-29.</p> <p>References:  Campanale 2020: The Crucial Role of Surgical Treatment in BIA-ALCL Prognosis in Early- and Advanced-Stage Patients. <i>Plast Reconstr Surg.</i> 2020 Nov;146(5):530e-538e.  Campanale 2018 (a): 22 Cases of Breast Implant-Associated ALCL: Awareness and Outcome Tracking from the Italian Ministry of Health. <i>Plast Reconstr Surg.</i> 2018 Jan;141(1):11e-19e.</p>	<p>P21line17. Reference of Campanale et al. 2020 is added.  Text adapted.  “However, but the recognition and timely diagnosis of BIA-ALCL is critical to prevent progression to more advanced disease that requires additional adjuvant systemic chemotherapy (Collins et al. 2019, Campanale et al. 2020). “</p> <p>P21 line27-29. SCHEER disagrees as these two statements are not considered contradictory. One concerns advice to remove contralateral implants, while the second text concerns possibilities for reconstruction/implantation.</p> <p>SCHEER disagrees, and sees these as two different subjects, being possibilities for reconstruction/implantation, and the advice to remove the contralateral implant in case of BIA-ALCL diagnosis. Also after removal of the contralateral implant, breast reconstruction and/or implantation may be needed.</p> <p>P21 line 54-55 has been adapted based on other comments:  “After surgery for BIA-ALCL, immediate or delayed breast reconstruction or further augmentation has been reported using implants or autologous tissue (Lamaris et al., 2019). The patient needs to be fully informed regarding current uncertainty about the safety of various types of breast implants with regards to BIA-ALCL and capsule formation.”</p>
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109	Geertsma Robert, RIVM - National Institute for Public Health and the Environment, Netherlands	4.6 Breast implant surface textures	<p>4.6 p.23, lines 31-37</p> <p>A revision of ISO 14607 is currently being initiated. Average surface roughness, surface area ratio and manufacturing method are recommended as important parameters by an International WG of regulators, representatives of breast implant registries and academics. Their report is expected to be published soon. The reference will be submitted to SCHEER as soon as it is available.</p>	<p>Thank you for this addition. SCHEER would gladly receive this report on surface characterization.</p>
110	Kerr Lisa, Therapeutic Goods Administration, Australia	4.6 Breast implant surface textures	<p>As part of a comprehensive review to evaluate the safety and quality of breast implants in relation to BIA-ALCL, the TGA Laboratories investigated the surface of 52 different models of breast implants and tissue expanders on the Australian register at the time. The types of shell surfaces tested were the following: open and closed salt loss, polyurethane (PU) foam, PU imprinting, sandblasted mandrel, gas diffusion (subsurface and surface).</p> <p>In addition to the features described in the SCHEER Opinion that characterise surface texture, the measurement of surface area ratio by use of micro-CT imaging is another important feature to determine surface complexity. Calculating roughness alone has its limitations as it underestimates the true surface topography, which may include overhanging or re-entrant features.</p> <p>For this reason, our recent work has identified the requirement to expand the classification system, by suggesting that the surface area is included in the surface description instead of applying a simple threshold on the surface roughness.</p> <p>For more detail, the report can be found published on the TGA website: <a href="https://www.tga.gov.au/biomaterials-and-engineering-laboratory-report-non-active-mammary-implants">https://www.tga.gov.au/biomaterials-and-engineering-laboratory-report-non-active-mammary-implants</a></p>	<p>The TGA report has now been included in section 4.6:</p> <p>“A recent TGA report has evaluated breast implants on the Australian market. (TGA 2019). The TGA concluded that the ISO method did not adequately describe the complexities of surface textures resulting from the myriad of texturing techniques manufacturers employ. Additionally TGA employed micro-Computed Tomography to extend the categories for surface characterization and was able to grouping of breast implants according to surface characteristics. These groupings include polyurethane-coated, closed salt-loss, open salt-loss, imprinting, subsurface gas diffusion, surface gas diffusion and smooth. It was concluded that the current classification systems require refinement and further examination to develop practical and clinical applications.”</p>
111	De Mezerville Roberto, Establishment Labs, Costa Rica	4.6 Breast implant surface textures	<p>RECOMMENDATION:</p> <p>There is an inconsistency between the texturing methods and the categories shown in the figure 1. The committee should clarify that imprint stamping produces LOW surface area and LOW roughness surfaces, and the process of turning inside out the shell produces nano-</p>	<p>SCHEER disagrees with the comment on the imprinting technique.</p> <p>The Figure 1 clearly indicates for “imprinting” a low surface area and low roughness.</p>

			<p>surface with MINIMAL surface area and roughness.</p> <p>Due to the fact that the above mentioned manufacturing processes can produce various surface roughness depending on the defined parameters and characteristics of the process, we consider necessary to separate the manufacturing processes from the surface area/roughness classification described in the figure. The determination of the classification should be based on the final shell topography characteristics.</p>	<p>Text has been adapted for clarity.</p> <p>“Imprint stamping with the process of turning inside out the shell can also produce low surface area and low roughness surfaces, including nano-surfaces with minimal surface area and roughness (Figure 1).”</p>
112	Sukop Andrej, Czech Society of Plastic Surgery, Czech Republic	4.6 Breast implant surface textures	<p>In evaluation of possible causality between the implant texture and the occurrence of BIA-ALCL, the ratio of the use of textured and smooth implants in the evaluated patient group/country/registry must be taken into account (in the Czech Republic, textured implants are used almost exclusively). Relevant information on what degree of texture is or is not connected to increased risk of ALCL is not currently available.</p>	<p>SCHEER agrees with the comment. But as this information is not available it cannot be included in the Opinion. Section 4.6 only gives an overview of the available surfaces and the techniques used to obtain an implant surface.</p>
113	Boegershausen Oliver, POLYTECH Health & Aesthetics, Germany	4.6 Breast implant surface textures	<p>not appropriate</p>  <p>Boegershausen_com ment_to_SCHEER_opi</p>	<p>SCHEER agrees with the comment that none of the proposals for classification of breast implant surfaces is related to clinical outcomes. This is already stated in section 4.6.</p> <p>“To date, none of the proposed surface texture classifications reported have been validated in a clinical study to determine which classification best predicts the risk of BIA-ALCL.”</p>
114	Brotherston Chris, GC Aesthetics, Ireland	4.6 Breast implant surface textures	<p>There is currently no universal or internationally accepted test method or definition of breast implant surface characteristics specifically linked to biological or clinical outcomes, although there continues to be significant discussion about such surface characteristics and their association with BIA-ALCL. There are currently many ways by which surface characteristics can be measured and described. Some investigators have used terms such as macrot textured and micro textured (De Boer et al, 2018, Barr et al 2017) whilst others have used the 3D and 2D classifications of surface area (Jones et al 2018, Rastogi et al 2019). These systems do not provide consistent data or comparison of product classification between manufacturers. Calobrace et al (2018) advise against ‘generalizing all implant texture as one in the same’ whilst discussing the risk of BIA-ALCL and compared it to the risk in general of other complications.</p>	<p>SCHEER agrees with the comments made. However, to date most if not all implants in BIA-ALCL cases are, as far as identified, textured implants. This indicates the importance of the characterization of the implant surface.</p> <p>SCHEER agrees that for each medical device the actual benefit-risk analysis should be leading for marketing authorization.</p>

		<p>While ISO 14607:2018 is considered the internationally recognised standard it also has limitations. In this standard the surface classification system is based on very broad categories of smooth, microtexture and macrotexture which are not based on specific biological or clinical attributes. The categories used have non-scientific origins e.g. the term “Macro Textured” originated from marketing terminology and not from a scientific perspective with data behind it. To fully describe implant surfaces a full rather than limited array of characteristics need to be taken into account as defined in the ISO standard which in Annex H.5 lists characteristics necessary to comprehensively describe surfaces including but not limited to pore size, diameter, kurtosis and skewness. Therefore, the use of surface roughness alone has limited use in defining breast implant surfaces effectively or for assessing their biological or clinical relevance. The international standard in Annex H.6 specifically states ‘...data resulting from the test at this point in time cannot be related to the performance or safety of the device...’</p> <p>The use of wide umbrellas to define implant surfaces does not take into account that all “macro” and “micro” textured surfaces are not the same both in terms of the surface roughness and other characteristics but also the different manufacturing processes and materials which are used by manufacturers.</p> <p>GC Aesthetics feel that all decisions should be made based on individual product safety outcomes and verified episode data rather than non-harmonised or necessarily unmeaningful texturing classifications which are not linked to safety. We would welcome the development of standardised characteristics of surface features linked to biological and clinical safety and performance. This harmonised characterization would allow biological and clinical research studies to be comparable without the confusion and inconsistency there is at present.</p> <p>References Barr S Hill EW Bayat A. Fuctional biocompatibility testing of silicone breast implants and a novel classification system based on surface</p>	<p>SCHEER agrees with the limitations of the ISO 14607:2018 surface characterization. Important aspects of implant surfaces were also addressed in the TGA 2018 report. Text has been added to section 4.6:</p> <p>“A recent TGA report has evaluated breast implants on the Australian market. (TGA 2019). The TGA concluded that the ISO method did not adequately describe the complexities of surface textures resulting from the myriad of texturing techniques manufacturers employ. Additionally TGA employed micro-Computed Tomography to extend the categories for surface characterization and was able to group breast implants according to surface characteristics. These groupings include polyurethane-coated, closed salt-loss, open salt-loss, imprinting, subsurface gas diffusion, surface gas diffusion and smooth. It was concluded that the current classification systems require refinement and further examination to develop practical and clinical applications.”</p> <p>And</p> <p>“ The ISO 14607:2018 is currently under revision as the classification based on surface roughness only was considered too limited as was also concluded in the TGA 2019 report.”.</p> <p>References have been included in appropriate parts of the Opinion.</p>
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			<p>roughness J Mech Behav Biomed Mater. 2017,Nov;(75): 75-81</p> <p>Calobrace MB, Schwartz MR, Zeidler KR, Pittman TA, Cohen R, Stevens WG. Long-Term Safety of Textured and Smooth Breast Implants. Aesthetic Surgery Journal 2018, Vol 38(1) 38–48</p> <p>De Boer M, van Leeuwen FE, Hauptmann M et al. Breast Implants and the Risk of Anaplastic Large-Cell Lymphoma in the Breast. JAMA Oncol 2018; 4; 335 – 341.</p> <p>Jones P, Mempin M, Hu H et al. The Functional Influence of Breast Implant Outer Shell Morphology on Bacterial Attachment and Growth. Plast Reconstr Surg 2018; 142; 837 – 849.</p> <p>Rastogi P, Riordan E, Moon D, Deva A. Theories of Etiopathogenesis of Breast Implant-Associated Anaplastic Large Cell Lymphoma. Plast Reconstr Surg 2019; 143; 23-29.</p>	
115	Parreira Carlos, EASAPS ESAPS, Belgium	4.6 Breast implant surface textures	We would like to point out that this chapter clearly shows that “textured” is not a scientifically appropriate term to cover all the different types of breast implants.	SCHEER agrees. Section 4.6 is an overview on textures as used for breast implants.
116	AYHAN SUHAN, GAZI UNIVERSITY FACULTY OF MEDICINE, TURKEY	4.6 Breast implant surface textures	<p>In the SCHEER report, it has been stated several times that a moderate causality between textured implants. However, BIA-ALCL seems to be a more complicated situation with the interaction of the native tissue with the surface of the foreign material, which is the breast implant in this scenario, along with the existence of the microorganisms and genetical predisposition of the patient. Therefore, it seems like the implant is not the only cause. Several findings suggest that the roughness, the cavities and spikes on the surface seems to create a chronic irritation that causes an inflammatory reaction triggering lymphocyte activation, proliferation and ultimately malignant transformation. The more aggressive the texturization is, the more bacterial colonization on the implant surface exists. A number of different systems have been proposed to classify implant surfaces, but none of those have been validated in a clinical study to determine which classification best predicts the risk of BIA- ALCL. 3-6</p> <p>Polyurethane (PU) coated implants deserve a few comments at this point. These implants are produced with a completely different technology compared to silicone surface implants. PU implants should</p>	<p>SCHEER agrees. However, the presence of a breast implant is necessary for the development for BIA-ALCL. In addition, to date most if not all implants in BIA-ALCL cases are, as far as identified, textured implants, or PU coated implants that have a high surface roughness. This indicates the importance of the role of the implant surface.</p> <p>Text has been added for better clarification. Abstract, Conclusions, Answer to Q5</p> <p>“A history of textured breast implants/expanders appears to be necessary but not sufficient for the development of BIA-ALCL”</p> <p>PU is separately mentioned in section 4.6 item d). d) polyurethane foam coating: refers to the application of an extra layer of foam coating to the implant.</p>

		<p>not be considered as textured implants because these implants do not pass a salt-loss, imprinting or any kind of texturization process. The polyurethane foam is a biocompatible three-dimensional matrix which is integrated with the implant shell via the process of vulcanization. This matrix also acts like a sponge, facilitating the absorption of the antibiotic solution and provides sustained antibiotic efficiency comparing to silicone surfaces which are more hydrophobic.</p> <p>According to the papers from Australia 7,8, polyurethane coated implants are classified as Grade 4 surfaces, even more than the Biocell surface, which is Grade 3. Using this classification, the risk of BIA-ALCL for Silimed PU implants are found to be 1:2596, and for Biocell implants 1:3194, based on the sales data in Australia and New Zealand 1. Nevertheless, this data cannot be used to generalize for all PU implants, for following reasons:</p> <ol style="list-style-type: none"> <li>1. We must remember that there are two brands for PU implants: Silimed (Brazil) and Polytech (Germany). Silimed implants are no longer available, since the factory has been shut down due to the technical compliance issues at Silimed’s manufacturing facility in Brazil. Production at Silimed stopped 2015 after European regulators found that the Silimed implants made at the factory displayed impurities on the surface. Specifically, they found cotton and silica particles that are used in the processing and manufacturing of implants. 9</li> <li>2. The production process of Silimed and Polytech implants are different (glueing vs vulcanization, respectively).</li> <li>3. The most common problem encountered in Silimed implants was delamination, which was not observed in Polytech implants for many years.</li> </ol> <p>It is obvious that we need more objective and prospective data to generalize the decisions for banning a wide spectrum of the implants. If this was the case, there should be hundreds of BIA-ALCL cases associated with PU implants all over the world, especially in South America where PU implants are most popular for decades.</p>	<p>Text added.</p> <p>“For breast implants with a polyurethane (PU) coated surface, it was suggested that they cannot be considered as macro-textured implants, even though, according to Figure 1, these PU coated implants do have a high surface area and high surface roughness (Hamdi 2019). For the PU coated Silimed implants the highest surface roughness and surface area was observed when various brands of breast implants were compared with each other (Jones et al. 2018). Also according to the ISO 14607 classification PU coated breast implants should be considered macro-textured.”</p> <p>The relation between Biocell and Silimed types of implants has now been specifically indicated in the Opinion.</p> <p>Text added to section 6.2 Conclusions.</p> <p>“As far as the manufacturer for textured implants was known most cases were found for the Biocell implant (texture manufactured by salt loss technique), while for PU coated breast implants BIA-ALCL cases were mainly associated with Silimed implant. Cases for other manufacturers were much lower. Although it cannot be considered to induce a textured surface on an implant, PU coating does result in an increase in surface area and roughness. The highest surface roughness and surface area was observed for PU coated Silimed implants, when various brands of breast implants were compared with each other (Jones et al. 2018).”</p> <p>For clarification on PU surfaces, text added in 4.6 Breast implant surface textures:</p> <p>“For breast implants with a polyurethane (PU) coated surface, it was suggested that they cannot be considered as macro-textured implants, even though, according to Figure 1, these PU coated implants do have a high surface area and high surface roughness (Hamdi 2019). For the PU coated Silimed implants, the highest surface</p>
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				roughness and surface area was observed when various brands of breast implants were compared with each other (Jones et al. 2018). Also, according to the ISO 14607 classification PU coated breast implants should be considered macro-textured.”
117	Mercer Nigel, Plastic, Reconstructive and Aesthetic Expert Advisory Group, United Kingdom	4.6 Breast implant surface textures	P23 Line 31-37 Conclusions. The assumption seems to be that texture is THE issue! This is not proven scientifically. As yet, the causal link to texture has not been proven. Comment should be made that not all manufacturers use the ISO classification and one manufacturer’s ‘smooth’ is another’s ‘micro’. The use of terms such as ‘smooth’ and ‘textured’ should cease in favour of the ISO descriptors of <50microns etc until we get a better classification.	SCHEER agrees. Section 4.6 is an overview on textures as used for breast implants.  Regarding the role of textured implants, text has been added for better clarification in: Abstract, Conclusions, Answer to Q5  “A history of textured breast implants/expanders appears to be necessary but not sufficient for the development of BIA-ALCL.”
118	Brotherston Chris, GC Aesthetics, Ireland	5.1 Literature searches	For the Attention of the SCHEER Committee   GC_Aesthetics_Scheer_Point_5.1_4_Dec_20  Please find our response to Point 5.1 The literature search done for the analysis was not properly planned and lacks transparency as to how the authors arrived to the final number of articles in Table 3. For example, if we replicate the first search on Pubmed and search for (Breast) AND (implant OR implants OR implantation OR lymphoma), without any filters except that of the time filter (i.e. from 2016 to 2019), there is a resulting 4,885 hits. Therefore, it can be difficult to understand how the authors went from 4,885 to 391 articles as they did not clearly specify inclusion/exclusion criteria nor filters used. Furthermore, there is no documentation as to how articles were selected. Indeed, as manufacturers we are held to a high standard when it comes to evaluating clinical data (as rightly should be the case) and we establish a search strategy template before a literature search can be done to ensure that no data is left out when	Thank you for the comment. There is a typo in Table 3 as well as in the text above it describing the search strategy. The search strategy should be:  (Breast) AND (implant OR implants OR implantation) AND (lymphoma)Article selection is in the WoE table including an evaluation of the various references/papers.

			<p>analysing device's safety. Therefore, we are critical as to how the authors selected their clinical data and believe a comprehensive search strategy should have been established for one to be confident in the resulting conclusion.</p> <p>A comprehensive analysis on the subject of textured implants should include both the risks and the benefits of its use. Therefore, the literature search should have highlighted both aspects. The incomplete overview of textured implants is reflected in the document itself. A simple search of the SCHEER preliminary opinion document shows that the word “benefit” is only mentioned twice and advantage once, while “textured” is mentioned 70 times and “risks” 71 times. Interestingly, an article by Calobrace et al. (2018) which discusses the long-term benefits of textured and smooth implants was noted as having been detected in the PubMed search but was not included in the analysis. Therefore, both the benefits and the risks of textured implants was not fully expanded upon and we believe a thorough analysis would be needed to understand the full scope of textured implants and its use.</p> <p>Another interesting note is that of the time filter. For example, when using the following keywords: (breast) AND (BIA-ALCL) and (implant), and searching for papers up until 2019, we find 108 results with the earliest papers published in 2013. Therefore, we question why September 2016 was selected as the starting point when normally literature searches would be at least 5 years, from Jan 2015-2020, or even 10 years.</p> <p>References  Calobrace MB, Schwartz MR, Zeidler KR, Pittman TA, Cohen R, Stevens WG. Long-Term Safety of Textured and Smooth Breast Implants. <i>Aesthetic Surgery Journal</i> 2018, Vol 38(1) 38–48</p>	<p>SCHEER is limited by the mandate. So, in certain areas benefit-risk evaluation is indicated in the Opinion. However, it was not the task of SCHEER to do a full benefit – risk assessment of textured implants. The mandate specifically asked for an evaluation on the role of breast implants in relation to BIA-ALCL.</p> <p>The paper of Calobrace et al. 2018 on long term evaluation of breast implants is cited in the Opinion. A text on the relative safety of breast implants is included in section 6.5.</p> <p>“Breast implants carry a reasonable assurance of safety and efficacy in that they perform as they were intended as indicated by the long term follow-up evaluated by Calobrace et al. (Calobrace et al. 2018).”</p> <p>Initially a starting point of September 2016 was used, as that was the end of the literature period that was included and evaluated in the previous SCHEER advice on BIA-ALCL.</p> <p>SCHEER: SCIENTIFIC ADVICE on The state of scientific knowledge regarding a possible connection between breast implants and anaplastic large cell lymphoma. 19 October 2017.</p> <p>But where appropriate, both older and more recent literature has now been included in the Opinion.</p>
119	No agreement to disclose personal	6. ASSESSME	General comment – chapter 6, assessment Could the SCHEER provide greater detail with respect to the quality of different data sources. For	All references that were collected based on the literature searches

	data	NT	<p>example, the Cordeiro et al. paper describes a risk estimate of 1:355 patients. It would be important to account for the median follow-up time for the different data sources identified, and other differences in quality of data.</p> <p>Many patients have &lt;5 years follow-up in clinical practice, and therefore having up to a 26 year follow-up with good completeness is important from a quality perspective. Without descriptions of completeness and a known median follow-up duration described it is challenging to compare rates.</p>	<p>and provided by the members of the WG were evaluated using the WoE methodology of SCHEER.</p> <p>SCHEER. Memorandum on weight of evidence and uncertainties Revision 2018. 26 June 2018.</p> <p>This information is indicated for the various references in the Opinion section 6.1 that described the studies included.</p>
120	No agreement to disclose personal data	6. ASSESSMENT NT	<p>General comment Could the SCHEER provide comment with respect to patients who may have a different perception of BIA-ALCL risk and risk acceptability?</p> <p>For example, patients who have reconstructive surgery following cancer diagnosis or patients with BRCA who have risk-reducing mastectomy may have a completely different perception of an additional BIA-ALCL risk than other populations.</p>	<p>SCHEER agrees that patient perception is very important. But, this does not belong to the remit of SCHEER.</p> <p>SCHEER has addressed the importance of patient involvement in section 4.1.</p> <p>Regarding implant choice:</p> <p>““Some trends are apparent in the literature for the use of one or another type of breast implant. However, the clinical indications for the use of a specific type of breast implant should depend on a consultation between clinician and patient to allow informed decision making to take place with regards to the choice of an appropriate breast implant. For breast reconstruction a shared consultation with a multidisciplinary healthcare team including a pathologist, oncologist, surgeon, breast care nurse, etc should be held with the patient to allow informed decision making to take place with regards to the breast reconstruction procedure as well as the choice of implant. For both aesthetic and reconstructive surgery all aspects of breast implants should be evaluated and discussed with the patient, expressly covering advantages, disadvantages, follow-up procedures and risk factors.”</p>



121	No agreement to disclose personal data	6.1 Epidemiology of BIA-ALCL	<p>Page 27, line 10-13 ‘In an analysis of BIA-ALCL cases throughout the world a substantial variation in reported incidences was evident, with the lowest rates being reported in the Eurozone, as well as China and Brazil, and the highest being reported in Australia and New Zealand. Reasons of this variation have not been clearly understood.’ Please provide a citation for the ‘analysis’ or clarify if this is based upon Brody, 2015.</p> <p>Could the SCHEER consider including a rationale with respect to the potential risk factors versus health system quality factors when comparing different data sources. For example, Australia has an opt-out system of registry, and AU/NZ have a national focus on this issue for some time.</p> <p>Systems for monitoring BIA-ALCL cases across Europe constitute a heterogeneous data-set and as such, the combination of these data-sets into one finding for the ‘Eurozone’ may be of limited validity, or would require greater clarification.</p>	<p>Page 27 line 10-13. Text is based on references above in section 6.1 itself.</p> <p>This is outside the remit of the SCHEER.</p>
122	Fleming Daniel, Australasian College of Cosmetic Surgery	6.1 Epidemiology of BIA-ALCL	<p>In addition to difficulties SHEER has already identified in the Preliminary Report, the Australian experience has shown that the numerator for estimating the incidence of BIA-ALCL is likely to be unreliable because of the pre and post testing eras and the ability of the disease to spontaneously regress, perhaps indefinitely. This rationale behind this experience also applies to the EU.</p> <p>The references below are from the uploaded scientific paper: Spontaneous Regression and Resolution of Breast Implant- Associated Anaplastic Large Cell Lymphoma: Implications for Research, Diagnosis and Clinical Management <i>Aesth Plast Surg</i> (2018) 42:672–678 available at <a href="https://doi.org/10.1007/s00266-017-1064-z">https://doi.org/10.1007/s00266-017-1064-z</a></p> <p>In Australia, the median time from implantation to diagnosis was 7.5 years, and 90% of the cases had occurred by 14 years[5, 11].</p> <p>Textured implants have been widely, and increasingly, used in Australia since 1991 yet the first case in Australia was not recognised until 16 years later. The testing of late seromas for cytology did not commence</p>	<p>SCHEER thanks Dr Fleming. The issue of spontaneous regression has now been included in the Opinion in section 4.5. However, this does not affect the reports cited in section 6.1. Section 6.1 described the epidemiology of BIA-ALCL as had been reported at the time of the report.</p>

		<p>until 2008 and has become increasingly common since. There is no reason to suppose that BIA-ALCL was not present with the same incidence in textured-implant-related late seromas prior to the advent of cytological testing as afterwards. This begs the question, where are the cases which should have</p> <p>been diagnosed in the interim? Cancer registry data have shown no increase in the incidence of non-Hodgkin lymphoma in women in the period 2000–2013 [23]. The existence of spontaneous regression and spontaneous resolution explains what happened to the seroma patients who had undiagnosed BIA-ALCL prior to the onset of cytological testing to look for it—they got better, often without surgical intervention [24, 25]. The inescapable conclusion is that the rapid and accelerating rise in the diagnosis of BIA-ALCL in Australia is just that—a rise in the diagnosis of the disease, not a rise in its incidence.</p> <p>This would not be unique. Observing the more than sixfold increase in the diagnosis of thyroid cancer without a change in mortality following the onset of screening in South Korea, the authors concluded, “over detection of clinically indolent thyroid cancers is the best explanation for the observed findings in our study” [26].</p> <p>These findings may not be unexpected as a pathological precedent for spontaneous resolution of a similar disease already exists. The spectrum disorder lymphomatoid papulosis and primary cutaneous ALCL is a rare skin disorder that is considered histologically malignant but often clinically benign [27]. Lesions contain atypical T cells that are also CD30+ and ALK-, as with BIA-ALCL [28]. The disease, which has been recognised since 1968, behaves similarly to BIA-ALCL in that it spreads infrequently and has an excellent prognosis. Importantly, it can spontaneously resolve, even in the primary cutaneous ALCL form [29].</p> <p>We ask that SCHEER consider this evidence in the context that WHO 2016 classification of BIA-ALCL as a new lymphoma was and remains, provisional. It is therefore, by definition, uncertain - a fact the implications of which have been largely ignored by the academic and lay media and indeed, thus far, regulators.</p>	<p>Every newly defined malignancy starts off as a ‘provisional’ entity in the WHO classification. For example, systemic ALCL was previously just one entity, which was then provisionally separated into ALK positive and ALK negative malignancies before being adopted as distinct entities in the 2016 WHO classification. Similarly, BIA-ALCL was first introduced in 2016 as a provisional entity but will become an established entity in the next revision of the WHO classification. In no way does this reflect that BIA-ALCL is “uncertain”. The provisional designation is there to reflect that we are not yet certain whether it is genetically distinct from other forms of systemic/nodal ALCL rather than whether it is a malignancy. It is indeed a bonafide malignancy as evidenced by multiple publications. Whether the term ‘lymphoproliferation’ or ‘malignancy’ is used to describe BIA-ALCL is purely a matter of semantics. All lymphoid malignancies are lymphoproliferations in that they are excess growths of lymphoid cells. What determines a malignancy as opposed to a benign growth is its ability to invade surrounding tissue. The fact that BIA-ALCL can invade into the capsule and in some cases the breast parenchyma very firmly places it in the category of a malignancy. Regardless, what is clear, is that left untreated, it can progress to a deadly disease.</p> <p>Text is modified for clarification.</p> <p>“In 2016, the World Health Organization (WHO) classified a number of</p>
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			<p>This has serious implications for patients who may be given the life-changing diagnosis of cancer when in reality they do not. We address this in more detail elsewhere in our submission.</p>	<p>lymphomas as provisional entities to distinguish these from other lymphomas, including BIA-ALCL which was associated with an excellent outcome when non-invasive disease stages are treated by surgical resection (Swerdlow et al., 2016)."</p>
123	CAMPANALE ANTONELLA, ITALIAN MINISTRY OF HEALTH, Italy	6.1 Epidemiology of BIA-ALCL	<p>p. 25 line 15-25: We would like to underline that the Italian experience and actions undertaken in order to promote awareness should be mentioned and commented. Indeed, in the paper The Crucial Role of Surgical Treatment in BIA-ALCL Prognosis in Early- and Advanced-Stage Patients. Campanale A, Spagnoli A, Lispi L, et al, we deal with the issue of the reliability of the numerator and denominator. We stated that variability of the incidence observed worldwide is attributable to all the factors that influence the numerator and the denominator in each country and we highlighted that by promoting the awareness of both physicians and patients, the accuracy of the numerator can be progressively improved. In order to increase the reliability of the denominator, the ImoH used sales breast implants data integrated with data from the arrangement of the Italian health care system in order to estimate the number of patients implanted with aesthetic and reconstructive purposes every year. Data from our vigilance activities let us to estimate the mean lifetime of the implant, that it is important to consider for the denominator estimation. The methodology used to estimate the denominator is explained in detail in "Reply: 22 Cases of Breast Implant-Associated ALCL: Awareness and Outcome Tracking from the Italian Ministry of Health. Campanale A, Boldrini R. Plast Reconstr Surg. 2018 May;141(5):779e.</p> <p>p. 25 line 30:In this paragraph, the WG reviewed the European studies without mentioning the Italian studies. Please add and comment the following reference: The Crucial Role of Surgical Treatment in BIA-ALCL Prognosis in Early- and Advanced-Stage Patients. Campanale A, Spagnoli A, Lispi L, et al. The ImoH is monitoring the incidence rate each year since 2015 and in this paper we have estimated the Italian incidence at approximately three in 100,000 implant patients per year. Although small oscillations were observed between 2015 and 2018, these are not statistically significant, and the disease remains a rare disorder.</p>	<p>P25 line 15-25. Text adapted to indicate the difficulties in obtaining reliable data.</p> <p>"There is a significant lack of knowledge of the actual total number of women with a breast implant, as it is rather difficult to obtain reliable data on the number of women with breast implants in the population for which sometimes sales data can give an indication (Campanale et al. 2018, De Boer et al. 2018)."</p> <p>Reference added : Campanale A, Boldrini R, Marletta M. 2018 22 Cases of Breast Implant-Associated ALCL: Awareness and Outcome Tracking from the Italian Ministry of Health. Plast Reconstr Surg. 2018 Jan;141(1):11e-19e.</p> <p>Text added to Page 25 line 30.</p> <p>"For Italy, the Italian Ministry of Health coordinated and centralized the collection of information on 46 cases of BIA-ALCL (Campanale et al. 2020). Confirmed cases must be notified to the Ministry of Health. Mean time of onset of symptoms was 6.4 ± 3.8 years (range 1 to 22</p>

		<p>p. 26 line 16-21: We believe that a comment should be added after this sentence in order to highlight that, to date, all studies in literature refer to the implant at the time of the diagnosis, and a lot of the data regarding clinical and implant history are declared as missing. We would like to stress the concept that Implant history is ALWAYS IMPORTANT in both circumstances when a smooth or textured implant is found in the patient clinical history, as to identify the right device implanted at the time of the onset of the first symptoms.</p> <p>In the paper “The Crucial Role of Surgical Treatment in BIA-ALCL Prognosis in Early- and Advanced-Stage Patients. Campanale A, Spagnoli A, Lispi L, et al., we highlight that in 62 percent of our patients with an implant history, the devices implanted at the onset of the symptoms were different from those identified at the time of the diagnosis, and among these, in 33 percent of cases, the manufacturer of the prosthesis observed at the time of diagnosis was different from the one implanted at the onset of the symptoms. In our population, textured breast implants have always been found at the first onset of the symptoms: 82.6 percent were macrot textured and 6.5 percent micro textured.</p> <p>Therefore, when we discuss about the involved devices, we must be sure that we are referring to the right one.</p> <p>We strongly feel that Authors NEED to recover and review the clinical history of all their reported cases, otherwise any effort to come to right the conclusion relative to the involved devices will be wasted.</p> <p>THIS ABSENCE OF DATA IS THE BIGGEST FAILURE OF THE RESEACH UNDERTAKEN IN THIS FIELD.</p>	<p>years) with a time to diagnosis of <math>7.2 \pm 3.7</math> years (range 2-22 years). Most of the patients (91%) demonstrated the presence of late seroma. For a non-disclosed active population, the incidence for Italy has been estimated as 2.8 per 100.000 patients receiving breast implants in 2015, 2.1 per 100.000 in 2016, 3.2 per 100.000 in 2017. and 3.5 per 100.000 in 2018. This disease was easily recognised as having a favourable prognosis even in advanced stages if complete surgical excision is performed. As reported 38 patients are free of disease, four are under follow-up, two had a recurrence 1 year later, and one patient died as result of an unrelated disease. The mean number of implants sold in Italy is approximately 51094 per year of which 95% have a textured surface. According to criteria of the International Organization for Standardization standard 14607:2018,17 at onset of first symptoms, the implant surface was macrot textured in 38 cases, micro textured in three cases, polyurethane in four cases, and unknown in one case. The history of previous implants was confirmed for 29 patients (63%) (Campanale et al. 2020).”</p> <p>P26line16-21. Text added:</p> <p>“ It should be noted that it is extremely important to evaluate the history of implants used in BIA-ALCL patients in order to identify a possible relationship with the implant brand and/or implant characteristics at the onset of disease (Campanale et al. 2020).”</p>
124	Mureau Marc, Erasmus MC Cancer Institute, University Medical Center Rotterdam, the	<p>6.1 Epidemiology of BIA-ALCL</p> <p>Very recently, the following very relevant, high-quality paper was published, which I feel should be discussed in this section.</p> <p>Nelson JA, Dabic S, Mehrara BJ, Cordeiro PG, Disa JJ, Pusic AL, Matros E, Dayan JH, Allen RJ Jr, Coriddi M, Polanco TO, Shamsunder MG, Wiser I, Morrow M, Dogan A, Cavalli MR, Encarnacion E, Lee ME, McCarthy CM.</p>	<p>Text added:</p> <p>“This study was extended to include 9373 patients over the period 1991-2017, of which eleven women developed BIA-ALCL all with a history of textured implants. The 26-year incidence of BIA-ALCL was reported as 1 in 559 (1.79 per 1000, 0.18%) patients and 1 in 871 (1.15</p>

	Netherlands, Netherlands		Breast Implant-associated Anaplastic Large Cell Lymphoma Incidence: Determining an Accurate  Risk. Ann Surg. 2020 Jul 16. doi: 10.1097/SLA.0000000000004179.	per 1000, 0.11%) textured implants (Nelson et al., 2020)."
125	MELVIN Tom, HPRA, Ireland	6.2. Epidemiology of BIA-ALCL based on data from Competent Authorities and Scientific Communities	Page 29, line 26-28 'The Netherlands reported a prevalence of 1:2,969, close to that observed in Australia which was 1:2,976. Both countries have a breast implant registry in which patients are registered by default, with the choice to opt out (Santanelli di Pompeo et al., 2020).' Considering the significant median time to onset identified by SCHEER, could the SCHEER provide a greater explanation of how they have accounted for the differences in duration of observation across registries, and how this may lead to an underestimation of the true incidence?	SCHEER agrees with the comment. However, as the time that registries have been implemented and used varies by country it is impossible to indicate how differences in duration of observation may have affected the results. For example it was reported by De Boer et al. 2018 that a diagnostic histopathology registry was used that existed since 1990. BIA-ALCL was observed by re-evaluating diagnosis in the pathology database whereby ALCL in the breast was taken as the diagnosis. So, this was not a specific BIA-ALCL database.  Consequently, the Australian study uses a database from which BIA-ALCL cases were evaluated.
126	Parreira Carlos, EASAPS ESAPS, Belgium	6.2. Epidemiology of BIA-ALCL based on data from Competent Authorities and Scientific Communities	Conclusions: Line 19 "Thus, the available data obtained from epidemiological studies, Competent Authorities and Scientific Societies, suggest that people with breast implants have a low absolute, but high relative risk of developing BIA-ALCL." Can you please clarify the "low absolute, but high relative risk"?  Line 27: "ISO (ISO 14607:2018) classified as macrot textured have been associated with a greater incidence of BIA-ALCL than microtextured." We all know that the majority are Biocell. Why not state this here? Better: "Biocell implants have been associated with a greater incidence of BIA-ALCL than microtextured."	A risk for cancer can be accepted if the risk is lower than 1 in a million. Compared to this figure a risk of 1 in 3000 for BIA-ALCL for breast implants is relatively high. If we consider the number of BIA-ALCL cases worldwide as approximately 1100, versus the millions of breast implants used, the absolute risk is thus low.  Allergan Biocell implants are mentioned in the description of the FDA data in section 6.2.  Text has been added to the conclusions of section 6.2.  "As far as the manufacturer for textured implants was known, most cases were reported in the context of a Biocell implant (texture by salt loss technique). For polyurethane coated breast implants BIA-ALCL cases were mainly associated with Silimed PU coated implant. Incidences for other manufacturers were much lower. Although they cannot be considered to induce a textured surface on an implant, PU coating does result in an increase in surface area and roughness. For the PU coated Silimed implants the highest surface roughness and

				<p>surface area was observed when various brands of breast implants were compared with each other (Jones et al. 2018).”</p>
127	Parreira Carlos, EASAPS ESAPS, Belgium	6.2. Epidemiology of BIA-ALCL based on data from Competent Authorities and Scientific Communities	<p>6.2. Epidemiology of BIA_ALCL based on data from Competent ... Line 21: “At the EU level, the EU Taskforce on Breast Implant Associated-ALCL composed of EU competent authorities received 398 BIA-ALCL reports (probable cases; some of these were unconfirmed cases due to the lack of actual testing). Out of these reports, 345 (86.7%) were confirmed cases of BIA-ALCL that meet the NCCN classification (Plymouth Meeting, PA, USA, <a href="https://www.nccn.org/">https://www.nccn.org/</a>) (Table 1). Table 4a – Confirmed cases of BIA-ALCL from EU member states and the UK (July 2020).”</p> <p>It was surprising to us to note that there is a EU European Taskforce but that the responsible of the registry of Sweden has never been contacted by anyone. While very many textured implants were used very few cases are reported. More information on this EU taskforce and how to contact them should be included.</p> <p>The E(A)SAPS taskforce “ALCL in Europe” chaired by Dr. Michel Rouif from France has been investigating the occurrence of confirmed cases of BIA-ALCL and deaths across Europe on a bi-annual basis, since 2017. E(A)SAPS actual data gathered from the last survey dated November 2020 on European confirmed cases indicate a total number of 425 cases and 14 deaths. The incidence of cases still differs highly across Europe and may be under-reported. Even though all countries are invited to report BIA-ALCL cases to the Patient Registry and Outcomes for Breast Implants and Anaplastic Large Cell Lymphoma Etiology and Epidemiology (PROFILE) registry/USA, the compliance of this register remains questionable. Reporting of confirmed BIA-ALCL cases to notified bodies still is not mandatory in all European countries. The total number of patients living with breast implants across Europe is not known. Moreover, the number of patients undergoing breast augmentation surgery for aesthetic or reconstructive reasons remains speculative. The denominator representing European sales rates of implants for aesthetic purposes is not validated. In addition, E(A)SAPS identified currently functioning breast implant registers in a limited number of European countries (Table 1). We would like to point out the</p>	<p>6.2 line 21.</p> <p>The information from Sweden is included in Table 4a as information obtained from the competent authorities, on the assumption that these authorities have a thorough overview of BIA-ALCL cases in their country.</p> <p>SCHEER recognises the input of E(A)SAPS but is disappointed that E(A)SAPS did not provide information when the call of information was launched by the European Commission’s Directorate General for Health and Food Safety.</p> <p>There was a public, open call for experts to participate and to submit information in the respective working group formed by SCHEER (<a href="https://ec.europa.eu/health/scientific_committees/call_experts/call_experts_bia_alcl_en">https://ec.europa.eu/health/scientific_committees/call_experts/call_experts_bia_alcl_en</a>), the deadline of which was actually extended once (from December 4th, 2019 to January 3rd, 2020) due to the low response received from experts.</p> <p>So, there has been ample opportunity for the public including scientific societies to provide information and comments and in doing so, to contribute to the SCHEER report.</p> <p>SCHEER agrees with the comment on the need for a European registry, and has included the need for the establishment of registries as one of its recommendations.</p>

			<p>need of an adequate National or European Breast Register for the indispensable follow-up of patients with breast implants.</p> <p>TABLE 1 Breast implant registers in European countries  Austria yes  France/Germany starting  Hungary yes  Netherlands yes  Spain yes  Sweden yes  Switzerland yes  UK yes</p> <p>The international initiative ICOBRA works intensively to align data for robust statistical analysis but extensive effort is still required. E(A)SAPS will contribute by offering countries without quality implant registers a standardized concept and will assist this initiative. There is a considerable bank of international data attributing a higher incidence of BIA-ALCL to macro-textured and polyurethane (PU) covered implants. Although, Allergan has withdrawn their products from the market, the next decade will show further the incidence of BIA-ALCL cases in patients with macro-textured and PU implants. In addition, data on risks for developing BIA-ALCL with other types of implant surfaces are sparse. The aforementioned aspects indicate that generalized epidemiological analyses and conclusions are weak when exclusively based on data from two populations, the Netherlands and Australia that are presented in the actual SCHEER report.</p> <p>Table 4b where is Australia?  Scientific Societies:  As emphasized above no AESTHETIC societies were contacted. Only EURAPS is mentioned. It is regrettable that our data which we collected since 2017 were not requested. What has been the methodology of selecting representative organisations?  Please add E(A)SAPS and our data in the next version of this document.</p>	<p>A Notified Body is not a regulatory institution.</p> <p>SCHEER agrees with this, and has already recommended the establishment of breast implant registries in its Advice on BIA-ALCL published in 2017.</p> <p>Data for Australia are presented above the table as information from the TGA. The cases in Table 4a are based on information from other Competent Authorities and Scientific Societies.</p> <p>An open call for both experts and data/information was launched, which did not result in a submission of data of E(A)SAPS.</p>
128	Decaluwé Kelly,	6.2.	Page 27 - Table 4a	

	The Federal Agency for Medicines and Health Products, Belgium	Epidemiology of BIA-ALCL based on data from Competent Authorities and Scientific Communities	In July 2020 the FAMHP had registered 13 cases of which certainly 12 cases are to be considered confirmed cases based on WHO criteria.	The data for Belgium has been adapted in Table 4a.
129	Mercer Nigel, Plastic, Reconstructive and Aesthetic Expert Advisory Group (PRASEAG), United Kingdom	6.2. Epidemiology of BIA-ALCL based on data from Competent Authorities and Scientific Communities	<p>P30: Conclusions: The uncertainty around BIA-ALCL data MUST be emphasised.</p> <p>BIA-ALCL was only recognised by WHO in 2016 and any data prior to this on prevalence and incidence has to be interpreted with caution because of of inherent diagnostic and underreporting reporting bias due to lack of professional awareness.</p> <p>It should be stated that BIA-ALCL risk calculations based on implant type/manufacturer also have to be interpreted with caution because the implant type/manufacturer denominator is not accurately known for over half of all cases of BIA-ALCL world wide. It is scientifically unsafe to link a case of BIA-ALCL causally with the implant in situ at presentation, unless it is the only implant to have been used in that anatomical site.</p> <p>P30 Line 20: (and P35, L36) The relative risk is irrelevant and would be confusing to patients. It should be removed.</p>	<p>Text has been adapted to indicate the uncertainty of these data:</p> <p>“Moreover, there is substantial variation in BIA-ALCL prevalence and incidence reported around the world, which may be attributed to the inherent diagnostic and underreporting bias due to a lack of professional awareness.”</p> <p>“The increase in incidence noted in more recent reports might be partially attributed to the increase of professional awareness and the establishment of uniform diagnostic criteria.”</p> <p>SCHEER disagrees that relative risk is not important. Most data give the relative risk a one case per X patients, the highest being 1 in approximately 3000 as observed in the Netherlands and Australia. Cordeiro et al. 2020 indicates in a study 1 in 355 in a specific group of patients. A follow up study on this study was reported by Nelson et al. 2020. Text modified to include follow up study of Nelson et al. 2020. Also the denominator is different in each case, e.g. women with any implant, women with Biocell implants etc.</p> <p>Text added.</p> <p>“This study was extended to include 9373 patients over the period 1991-2017, of which eleven women developed BIA-ALCL, all with a</p>



				history of textured implants. The 26-year incidence of BIA-ALCL was reported as 1 in 559 patients and 1 in 871 textured implants (0.11%) (Nelson et al., 2020).”
130	Mercer Nigel, Plastic, Reconstructive and Aesthetic Expert Advisory Group (PRASEAG), United Kingdom	6.2. Epidemiology of BIA-ALCL based on data from Competent Authorities and Scientific Communities	<p>P27 Line 35: ‘of them’ should be replaced by ‘of these’.</p> <p>P28 Line 12-13: It is not helpful to highlight publications that state of 686 cases 90% were Allergan with-out giving data about manufacturers’ volume of sales. This introduces bias. It has to be assumed that BIA-ALCL will occur with all breast implants. No implants should be described as ‘safe’.</p> <p>In the current state of knowledge it is better to say BIA-ALCL is associated with breast implants, in particular textured implants (surface roughness &gt;50microns) and BIA-ALCL risk appears to increase with roughness of texturing.</p> <p>P29 Line 3: It must be made clear that the recall was of stock on shelves, not from previously implanted patients and that no regulatory agency is recommending the removal of the implants from patients because the individual risk is smaller than the risk of removal. In addition, what does is used to replace the implant. It cannot be stated categorically that smooth implants are ‘safe’ because ALCL has been associated with smooth breast implants inserted in other anatomical sites.</p>	<p>P27 line 35. Text changed.</p> <p>SCHEER agrees. But it is highly suspect that of all the cases in which the implant brand was identified such a high proportion were of the Allergan Biocell model. These are data stated on the FDA website. Similar data from Australia indicate a high percentage of BIA-ALCL cases to be found near Silimed PU coated implants.(Loch-Wilkinson et al. 2020)</p> <p>SCHEER agrees. Text with this meaning is already presented in section 6.4 including: “The common characteristic is the presence of a textured breast implant suggesting an aspect of these particular devices is causative, whether that be direct or indirect.”</p> <p>SCHEER agrees with the comment. The presence of other implant associated ALCL has indeed been reported several times but only as incidental individual cases. This is in strong contrast with the frequent cases reported for BIA-ALCL.</p> <p>Text on withdrawal has been adapted: “The recall was for implants in stock that had not yet been implanted in patients. The removal of Biocell implants in situ is not recommended in view of the relative low risk of BIA-ALCL.”</p>
131	No agreement to disclose personal data	6.2. Epidemiology of BIA-ALCL based on data from Competent	In the discussions about the risk assessment BIA-ALCL I came to do an initial exercise of the number of women with breast implants worldwide. I shared that information with a couple of people but I cannot publish that information because the sources to substantiate the numbers are not cooperative in their confirmation.	SCHEER has reported the highest risks as indicated in the paper published by Cordeiro et al. 2020, and the follow up study by Nelson et al. 2020. Other studies present the risk with the highest risk as 1 in

	<p>Authorities and Scientific Communities</p>	<p>After the 2nd Consensus Conference and the SCHEER hearing I went to investigate on the specific number of Biocell implants placed worldwide and get to a risk assessment for BIA-ALCL in a worst case scenario.</p> <p>Background: Biocell implants were introduced in the late 80's by McGhan Medical, later that became Inamed before it was purchased by Allergan. Biocell has been around for 30 years and has been market leader for most of that time.</p> <p>Estimation: I estimate that 15 million Biocell implants have been placed in 8.2M women worldwide. Considering a drop out of 30% due to removal, replacement, death by natural cause we are still looking at 5.8-6.0M women with Biocell implants.</p> <p>Risk Assessment: The latest published number of BIA-ALCL cases is 1.136 of which 85% or approx. 1.000 are with Biocell implants (assuming each case is with one woman only) If the number of 1.000 is used on the number of women with Biocell you would get a current risk of 1:6.000 However, if you would take the risk assessment of Peter Cordeiro's 2020 JPRAS publication where he diagnosed BIA-ALCL in 1 in 350 of his 3.546 patients cohort all with Biocell implants, the expected number of women who might develop BIA-ALCL is around 17.000 (6.0M divided by 350).</p> <p>Comments: No matter how you assume the numbers there are still a lot of women out there running a risk for developing BIA-ALCL and are not aware of this (the number is still 12.000 if there are only 4M women with Biocell implants) If we currently have 39 women who died because of BIA-ALCL we can estimate that that number is going to increase by 15 to 20 times if we don't create early detection and better awareness around the disease. I understood from the last conference that the number in Cordeiro's</p>	<p>approximately 3000 women with breast implants in Australia and the Netherlands.</p> <p>SCHEER recognises that the relationship with textured (Biocell) implants and although less in number for certain PU coated implant (Silimed) has been clearly established. But not all textured implants have been associated with BIA-ALCL, and the discussion regarding smooth implants is ongoing, although at the time of this report only one confirmed BIA-ALCL case has been reported exclusively in the context of a smooth implant.</p>
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			<p>paper increased by 8 so the total is now 18 on 3.546 which is 1 in 200 of his patients, this number however needs confirmation.</p> <p>Fact In Cordeiro's paper 5 of the 10 diagnosed cases were prophylactic mastectomies, women seeking safety by getting their breast tissue removed and, in looking for that security, receiving a man-made lymphoma. Currently the women contacting our service present at a ratio of 1 in 5 will test positive, this is a startling number and needs to be addressed. The risks need to be transparent and screening needs to be introduced to minimise the long term risk. Consultant breast surgeons need to be aware of the risks and stop dismissing it as a rare disease, its not rare , its emerging. We strongly advise ALL textured implants to be banned and patients safety is above profit .</p>	
132	CAMPANALE ANTONELLA, ITALIAN MINISTRY OF HEALTH, Italy	6.2. Epidemiology of BIA-ALCL based on data from Competent Authorities and Scientific Communities	<p>p. 27 line 33-36: These conclusions are biased by the fact that the WG is considering the devices implanted at the time of diagnosis disregarding if a complete implant history exists. We would like to stress the concept that Implant history is ALWAYS IMPORTANT in both circumstances when a smooth or textured implant is found in the patient clinical history, as to identify the right device implanted at the time of the onset of the first symptoms.</p> <p>p.28 line 8: Please add and comment the reference published on the Italian Ministry of Health webpage on the BIA-ALCL: Protesi mammarie e Linfoma anaplastico a grandi cellule (ALCL) (salute.gov.it)</p> <p><a href="http://www.salute.gov.it/portale/temi/p2_6.jsp?id=4419&amp;area=dispositivi-medici&amp;menu=vigilanza">http://www.salute.gov.it/portale/temi/p2_6.jsp?id=4419&amp;area=dispositivi-medici&amp;menu=vigilanza</a></p> <p>p. 29 line 20-28: In this paper (Santanelli Di Pompeo 2020) the estimation of the BIA-ALCL prevalence in Europe, although well described and overall correct, has some limitations. In particular, a major limit is to consider the same diffusion of breast implants in all the EU-28 countries (i.e., 3% of the population). Actually, this value (that represents the denominator of the prevalence rate) was observed only</p>	<p>P27line33-36 SCHEER agrees with the comment. The issue of importance of implant history is addressed elsewhere in the Opinion, section 6.1.</p> <p>“It should be noted that it is extremely important to evaluate the history of implants in the BIA-ALCL patients in order to identify a possible relationship with implants brand and/or implant characteristics at diagnosis (Campanale et al. 2020).”</p> <p>P28 line8. The paper of the Italian Ministry of Health is now cited in the text.</p> <p>“For Italy the Italian Ministry of Health coordinated and centralized the collection of information on 46 cases of BIA-ALCL (Campanale et al. 2020). Confirmed cases must be notified to the Ministry of Health. Mean time of onset of symptoms was <math>6.4 \pm 3.8</math> years (range 1 to 22 years) with a time to diagnosis of <math>7.2 \pm 3.7</math> years (range 2-22 years).</p>

		<p>in two countries (Holland and Italy). Is it plausible that this percentage is the same in all the European countries despite cultural diversities and differences in mean age? Moreover, Italian data were unpublished. Another limitation is the fact that the authors did not clearly explain if any standardization technique has been used to stratify the proportion of breast implants among different age groups. It can only be assumed that this aspect has been covered. Finally, it should be noted that this paper is based on the existing literature (which is mostly represented by low level of evidence) and on the available data, making the overall estimate biased. The (presumed) lack or incorrectness of data collection from some countries and the limited literature references have produced a work of poor scientific evidence (level IV), published in a peer-review journal whose main topic is aesthetic surgery.</p> <p>p.30 line 28-30: THIS ABSENCE OF DATA IS THE BIGGEST FAILURE OF THE RESEACH UNDERTAKEN IN THIS FIELD. It is unfair and speculative to recall the importance of a previous implant history only when a smooth device has been found at the time of diagnosis. in both circumstances when a smooth or textured implant is found in the patient clinical history, as to identify the right device implanted at the time of the onset of the first symptoms.</p> <p>p.30 line 30-32: This sentence is in contradiction with the sentence in page 32 line 15-16 “All patients had a history of a textured device; there were no patients who had a smooth-only device history”</p>	<p>Most of the patients (91%) demonstrated the presence of a late seroma. On a non-disclosed population the incidence for Italy has been estimated as 2.8 per 100.000 patients receiving breast implants in 2015, 2.1 per 100.000 in 2016, 3.2 per 100.000 in 2017. and 3.5 per 100.000 in 2018. The disease was easily recognised with a favourable prognosis also in advanced stages if complete surgical excision is performed. As reported 38 patients are free of disease, four are under follow-up, two had a recurrence 1 year later, and one patient died as result of an unrelated disease The mean number of implants sold in Italy is approximately 51094 per year of which 95% has a textured surface. According to criteria from the International Organization for Standardization standard 14607:2018, at the onset of the first symptoms, the implant surface was macrot textured in 38 cases, microtextured in three cases, polyurethane in four cases, and unknown in one case. The history of previous implants was confirmed in 29 patients (63%) which showed that the devices involved at the time of the onset of symptoms were different from those implanted at the time of diagnosis in 18 cases (62 percent) (Campanale et al. 2020). “</p> <p>P29 line 20-28. SCHEER agrees with the comment regarding the limitations of the Opinion in respect to data availability. The figures presented are based on the references Santanelli di Pompeo 2020 that was based on official data from the European Association of Plastic Surgeons, and De Boer et al 2018 on BIA-ALCL cases in the Netherlands. SCHEER is aware that high level of evidence studies e.g. prospective randomized clinical studies are almost impossible to do in view of the long latency period of BIA-ALCL. A retrospective case control study is at the moment one of the best possibilities to determine causal relationship. SCHEER also suggests the initiation of breast implant registries that would make data mining into BIA-ALCL cases and their history possible for the future.</p>
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				<p>For the moment, SCHEER, as an independent scientific advisory body, can only report with transparent arguments in its Opinions that are based on publicly available information/literature.</p> <p>P30 line 28-30. The importance of obtaining information regarding the implant history of the patient is indicated in the text above.</p> <p>P30 line 30-32 and P32 line 15-16. SCHEER disagrees. Page 32 only discusses cases in the PROFILE registry, so there is no contradiction with the text on page 30 that refers to one FDA reported case of an exclusively smooth implants associated BIA-ALCL.</p>
133	Garson Sebastien, SNCPRE, France	6.2. Epidemiology of BIA-ALCL based on data from Competent Authorities and Scientific Communities	<p>page 27 line 35: Can you warranty which texture gives the BIA ALCL? Do these datas are the implant texture at the time of the diagnose?</p> <p>In France for exemple they take for responsible the last implant put in and mis understood the story of the implant because for France 1/3 are primary implantation 1/3 are two and 1/3 more than 2. In practice it's very difficult to get the all clear story and only 2/3 of the French cases are significant. Do you have the same experience in the other country?</p> <p>If so these stats are not significant.</p>	<p>P27 line 35. These data represent the implants present at the time of diagnosis.</p> <p>SCHEER has no experiences of practices used in other countries. SCHEER relies on the published literature and data provided by professional organisations.</p> <p>In view of the fact that the denominator in most studies is lacking, statistics cannot be properly performed and therefore cannot be discussed in this report.</p>
134	No agreement to disclose personal data	6.3 Epidemiology of BIA-ALCL based on reports obtained	<p>Page 30 Lines 14-15 'of note, a few earlier studies, prior to 2017, have reported zero cases BIA-ALCL, suggesting no association'. It is not clear which papers are referred to here as there are no references presented. In the context of the conclusions elsewhere in the preliminary opinion on the strong association identified between breast implants and ALCL and in view of the widespread acknowledgement that the awareness of this condition has increased dramatically over the past decade, this</p>	<p>The references are discussed in the section above the conclusions (Vase et al., 2013). It was not deemed necessary to again cite the references in the conclusion section.</p>

		from registries	conclusion that published historic data suggests ‘no association’ may be confusing in the context of the remainder of the opinion, and further qualification of this conclusion could help.	
135	No agreement to disclose personal data	6.3 Epidemiology of BIA-ALCL based on reports obtained from registries	<p>Page 30 Lines 13-14 The relative risk (odds) of those with breast implants developing BIA-ALCL varies from 18.2 to 421.8 The HPRA would prefer greater clarity on the source of the data for the range that has been presented. The 2018 Odds Ratio (421.8) appears to be an updated calculation (2009 Odds Ratio (18.2)) from the same data set analysed over a longer time period. Both appear to have the same starting date (1990).</p> <p>It may be more accurate to reflect that over the period 2009 to 2018, the calculated odds ratio increased from 18.2 to 421.8.</p>	<p>The variation indicated in the text for the odds ratio is based on data presented in the cited literature page 30, lines 5-7.</p> <p>As the odds ratio varies over the years, it would not be correct to suggest an increase. As stated in this comment, the increase might not be a true increase but a result of the improved awareness of professionals dealing with BIA-ALCL cases and improved diagnostic techniques.</p>
136	No agreement to disclose personal data	6.3 Epidemiology of BIA-ALCL based on reports obtained from registries	<p>Page 30 Lines 7-12 the lifetime incidence of BIA-ALCL varies from 1.65 cases per 100,000 women with implants to 35 cases per 100,000 women with implants (for comparison reasons, the incidence of breast cancer in the world in 2018 was estimated to be 2,088.8 cases per 100,000 women aged 0-74 years, and the incidence of non-Hodgkin lymphoma in women was 224.9 cases per 100.000 women (Ferlay et al., 2018); while in Europe, the incidence of breast cancer was estimated 1,195.2 cases per 100,000 women (Heer et al., 2020)) The HPRA considers that the use of breast cancer and non-hodgkin lymphoma as comparator incidences here would benefit from greater explanation.</p> <p>As identified in the preliminary opinion, there is moderate evidence of a causal relationship between textured breast implants and BIA-ALCL. The HPRA would consider it more relevant to provide a comparator incidence for the rate of ALCL in the breast in individuals without breast implants.</p> <p>Alternatively, it may be of greater relevance to describe the incidence rates for situations where an iatrogenic intervention, or an environmental or occupational exposure, has resulted in an increased</p>	<p>These two comparison are included to put the risk of BIA-ALCL in perspective and to indicate that the BIA-ALCL risk is (very) low. BIA-ALCL can easily be avoided by not implanting a breast implant while not all other cancer risks are as easily mitigated.</p> <p>The incidence of ALCL in the breast is presented in the paper of De Boer et al. 2018 in their retrospective evaluation of a histopathology database in the Netherlands. De Boer et al. identified 42 cases of ALCL in the breast over a period of 26 years, of which 32 were associated with a breast implant.</p>

			incidence of cancer.		
137	Parreira Carlos, EASAPS ESAPS, Belgium	6.3 Epidemiology of BIA-ALCL based on reports obtained from registries	Line 22: “Alternatively, in the absence of a breast implant registry, cases of BIA-ALCL could be included in a dedicated disease-specific (e.g., cancer) registry “  Better in our opinion would be to report to the National notifying body that reports to the EU ALCL Taskforce: “Alternatively, in the absence of a breast implant registry, cases of BIA-ALCL should be reported to the National notifying body that reports to the EU ALCL Taskforce “		A disease specific registry was included based on experience in the Netherlands in which the histopathology database provided valuable information on BIA ALCL diagnosis over a period of 26 years.  The text above the conclusion section clearly identifies other types of registries, besides a breast implant registry, as information sources for BIA-ALCL.
138	CAMPANALE ANTONELLA, ITALIAN MINISTRY OF HEALTH, Italy	6.3 Epidemiology of BIA-ALCL based on reports obtained from registries	p.31 line 1-2: Italy has its own National breast implant registry since March 2019. Please add and comment the following paper that shows the current situation of breast implant registry worldwide. Moving breast implant registries forward: Are they FAIR and Functional? Bargon CA, Becherer BE, Young-Afat DA, et al. J Plast Reconstr Aesthet Surg. 2020 Oct 17;S1748-6815(20)30498-8. doi: 10.1016/j.bjps.2020.10.001. Online ahead of print.  p. 31 line 25-38:The IMoH has created a specific registry of BIA-ALCL patients. This has been reported two years ago in the paper “22 Cases of Breast Implant-Associated ALCL: Awareness and Outcome Tracking from the Italian Ministry of Health. Campanale A, Boldrini R, Marletta M. Plast Reconstr Surg. 2018 Jan;141(1):11e-19e., and restated in the papers “The Crucial Role of Surgical Treatment in BIA-ALCL Prognosis in Early- and Advanced-Stage Patients” Campanale A, Spagnoli A, Lispi L, Boldrini R, Marletta M. Plast Reconstr Surg. 2020 Nov;146(5):530e-538e.  Please cite and comment the above papers.		Text has been added on page 31:  “The current status of breast implant registries worldwide is presented in Bargon et al. 2020”  and  “In Italy the Ministry of Health has created a specific registry for BIA-ALCL patients (Campanale et al., 2018, 2020).”
139	BENITO-RUIZ JESUS, ANTIAGING GROUP	6.3 Epidemiology of BIA-ALCL	lines 4-6 Comment: your statement is not updated. Both national societies from Spin (AECEP and SECPRE) are members of ICOBRA as well.		Spain has been added to the listing.

	BARCELONA, Spain	based on reports obtained from registries		<p>The ICOBRA specific reference has been added.</p> <p>Spronk PER, Begum H, Vishwanath S, Crosbie A, Earnest A, Elder E, Lumenta DB, Marinac-Dabic D, Moore CCM, Mureau MAM, Perks G, Pusic AL, Stark B, von Fritschen U, Klein H, Cooter RD, Rakhorst HA, Hopper I. Toward International Harmonization of Breast Implant Registries: International Collaboration of Breast Registry Activities Global Common Data Set. <i>Plast Reconstr Surg.</i> 2020 Aug;146(2):255-267. doi: 10.1097/PRS.0000000000006969.</p>
140	Geertsma Robert, RIVM - National Institute for Public Health and the Environment, Netherlands	6.4. Mediating and/or moderating factors associated with the risk of BIA-ALCL	6.4 p.34. lines 27-32 Agreed! So, how does SCHEER substantiate general statements on a causal relationship of (all) textured implants? (see previous comments)	<p>The text on textures of implants has been modified.</p> <p>Abstract, Conclusions section 2, Answer to Q5</p> <p>“Overall SCHEER considers that there is a moderate weight of evidence for a causal relationship between textured breast implants and BIA-ALCL, particularly in relation to implants with an intermediate to high surface roughness.</p> <p>At this point it should be noted that i) there are several types of textured implants ii) surface textures of breast implants are not all manufactured in the same way, and iii) implants with diverse surface textures may also present different benefits. The magnitude of the risk per type of textured implant is difficult to establish due to the low incidence of the risk. Even with macro-textured implants, BIA-ALCL has a very low incidence. Therefore, risk assessments per implant type are needed. Furthermore, the risk should be weighed against the benefits. There is also a need for an unambiguous, clinically validated classification system for breast implants including more parameters than just “surface roughness”. A history of textured breast implants/expanders appears to be necessary but not sufficient for the development of BIA-ALCL.”</p>



141	Brotherston Chris, GC Aesthetics, Ireland	6.4. Mediating and/or moderatin g factors associated with the risk of BIA- ALCL	<p>For the Attention of the SCHEER Committee</p>  <p>GC_Aesthetics_Scheer_Point_6.1_4_Dec_20</p> <p>Please find our response to Point 6.4</p> <p>At this time the aetiology of BIA-ALCL is not clear (Fitzal et al, 2019) although there could be links to Biofilm and genetic disposition.</p> <p><b>Biofilm Formation and its Influence on BIA-ALCL</b> Recent studies have indicated that the aetiology of BIA-ALCL may involve infection and the development of biofilms. Studies have shown that infections may cause inflammation surrounding a breast implant and cause increased rates of capsular contracture (Nava et al 2017). In the same way that the formation of biofilms may play a role in the inflammatory response that leads to the formation of capsular contracture. A leading theory is that an increased inflammatory response to the presence of bacteria can cause seroma to form and further cause immunological responses leading to the development of ALCL (Ramos-Gallardo et al 2016, Clemens et al 2016).</p> <p>Since the presence of bacteria/ biofilms may play a significant role in the development of ALCL, further study is required to determine if this is a primary cause or multifactorial.</p> <p><b>Genetic Predisposition and its role in BIA-ALCL development</b></p> <p>Many studies have been published on a genetic predisposition to developing BIA-ALCL. Genomic and functional characterisation of systemic ALK-negative ALCL has revealed the importance of STAT3 activation, MYC expression, PRDM1/TP53 abnormalities and recurrent structural variants. As it stands, the genomic landscape of BIA-ALCL and its relevant pathogenic drivers are significantly less well characterized (Mehta-Shah et al 2018). To further complicate matters, a combination of textured breast implant, bacterial contamination and genetic predisposition appears to be necessary for BIA-ALCL to occur (Groth and</p>	<p>The Fitzal et al 2019 reference has been included to the reference list.</p> <p>Text added:</p> <p>“ Some studies have indicated that the aetiology of BIA-ALCL may involve infection and the development of biofilms. Infections may cause inflammation surrounding a breast implant and cause increased rates of capsular contracture (Nava et al 2017). It might be that an increased inflammatory response to the presence of bacteria can cause a seroma to form and further induce immunological responses leading to the development of ALCL (Ramos-Gallardo et al 2016, Clemens et al 2016).”</p> <p>SCHEER agrees with the comment and has included this aspect in section 6.4. The reference Mehta-Shah et al 2018 refers to two case reports of BIA-ALCL and only suggests genetic factors in the predisposition of BIA-ALCL.</p> <p>In the conclusion of section 6.4, the following is stated:</p> <p>“None of the proposed hypotheses are necessarily mutually exclusive. A combination of textured breast implant, bacterial contamination, and genetic predisposition has been suggested as necessary for BIA-ALCL to occur (Groth and Graf 2019). However, the presence of chronic inflammation, no matter what causes it, might drive lymphomagenesis by multiple pathways.”</p> <p>Regarding the comment on multiple origin the text has been adapted.</p> <p>“None of the proposed hypotheses are necessarily mutually exclusive.</p>
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			<p>Graf, 2019). Turner (2019) states that BIA-ALCL development is very likely a spectrum of mechanisms amongst patients, with allergy and autoimmunity providing conducive backgrounds for chronic stimuli whether of bacterial and/or synthetic origins.</p> <p>References  Clemens MW, Nava MB, Rocco N &amp; Miranda R. Understanding Rare Adverse Sequelae of Breast Implants: Anaplastic Large-Cell Lymphoma, Late Seromas, and Double Capsules. <i>Gland Surg</i> 2016; 10; 21-37.  Fitzal F, Turner SD, Kenner L. Is breast implant-associated anaplastic large cell lymphoma a hazard of breast implant surgery? <i>Open Biol</i> 2019 9:190006  Groth, K., and Graf, R. Breast implant-associated anaplastic large cell lymphoma (BIA-ALCL) and the textured breast implant crisis. <i>Aesth Plast Surg.</i> 2020; 44; 1-12.  Mehta-Shah N, Clemens MW, Horwitz S. How I treat breast implant-associated large cell lymphoma. <i>Blood</i>, 1 Nov 2018, Vol 132 (18) 1889-1897  Nava MB, Rancati A, Angrigiani C, Catanuto G &amp; Rocco N. How to Prevent Complications in Breast Augmentation. <i>Gland Surg.</i> 2017; 6; 210-217.  Ramos-Gallardo G, Cuenca-Pardo J, Rodríguez-Olivares E, Iribarren-Moreno R, Contreras-Bulnes L, Vallarta-Rodríguez A et al. Breast Implant and Anaplastic Large Cell Lymphoma Meta-Analysis. <i>J Invest Surg</i> 2016; 00; 1-10.  Turner, S., Inghirami, G., Miranda, R., &amp; Kadin, M. Cell of origin and immunological events in the pathogenesis of breast implant-associated anaplastic large cell lymphoma. <i>American J Pathol.</i> 2019.  <a href="https://doi.org/10.17863/CAM.44012">https://doi.org/10.17863/CAM.44012</a></p>		<p>A combination of textured breast implant, bacterial contamination, and genetic predisposition was suggested to be necessary for BIA-ALCL to occur (Groth and Graf 2019). However, the presence of whereby chronic inflammation, no matter what causes it, might drive lymphomagenesis by multiple pathways.”.</p>
142	Fleming Daniel, Australasian College of Cosmetic Surgery, Australia	6.4. Mediating and/or moderating factors associated with the	<p>We agree with the preliminary report's conclusion that chronic inflammation is necessary for the development of BIA-ALCL. The references herein are taken from the uploaded article. Australia has reported the highest per capita incidence of BIA -ALCL. The highest incidence has been observed with salt-reduced macrot textured implants (Allergan Biocell and Nagor textured) and delaminated, faulty Silimed polyurethane foam covered (PU) implants, both of which are</p>		<p>SCHEER is familiar with the issue of both the Biocell Allergan implant in relation to the surface roughness, and the Silimedimplant.</p>


	<p>risk of BIA-ALCL</p>	<p>known to shed more particles than those implants with lower rates of BIA-ALCL [15, 22], including implants with similar surface areas.</p> <p>The hypothesis that bacterial load proportional to the surface area of the implant is the cause of BIA-ALCL does not fit the evidence. For it to be true requires that all PU silicone breast implants will have the highest incidence of BIA-ALCL as they have the greatest surface area. However, only one brand of PU implants, Silimed, currently has such a reported increased incidence. Silimed are known to cause increased inflammation through delamination of the PU foam layer and particle shedding, as a consequence of a manufacturing fault [15]. An example of delamination and particle shedding is shown in Fig. 1.</p> <p>The only other brand of PU implant available, Polytech, does not have any such known manufacturing fault and at the time of publication of the attached paper, has only a single case of BIA-ALCL in Australia one other worldwide. Accordingly, it has been reported to have currently the lowest incidence of BIA-ALCL for a ‘textured’ implant [16]. This is at odds with the infection theory and unless numbers of cases of BIA-ALCL related to Polytech PU implants dramatically increase, the hypothesis that bacterial contamination proportionate to implant surface area is the cause of BIA-ALCL will be disproved.</p> <p>It may be relevant that properly constructed PU implants are the most likely to adhere and remain adherent to the implant capsule. thus they do not rub against the capsule and cause further inflammation through friction.</p> <p>Supporters of the bacterial theory argue that particles cannot cause BIA-ALCL as a biological mediator (they argue only bacteria) is necessary to initiate lymphomatoid change. However, all patients with implants will inevitably be exposed, either at the time of surgery or subsequently, to some form of biological mediator, either bacterial and/or viral, capable of mediating a lymphomatoid change at the cellular level.</p> <p>In this context, currently, the evidence supports a chronic inflammation threshold must be exceeded in genetically susceptible individuals in the</p>	<p>SCHIEER has now added to the report that BIA-ALCL is primarily associated with two specific types of breast implants: the Biocell-Allergan type and the Silimed bPU-coated breast implant.</p> <p>However, it should be noted that even though the Biocell implant represents the highest percentage when considering BIA-ALCL cases reported to date, cases have also been reported in the context of other brands and types of textures.</p> <p>Until proven otherwise, the bacterial contamination/infection theory remains one of the possible aetiological associations for BIA-ALCL.</p> <p>In the conclusion, the potential for multiple causes for the induction of BIA-ALCL is discussed. However, the chances for ALCL in the breast without an implant is far lower as demonstrated by De Boer et al., 2018.</p> <p>SCHIEER is aware of the differences between the two PU coated implants that are/were available on the market. This was also clearly commented upon by the manufacturer of Polytech breast implants.</p>
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			<p>presence of a bacterial or viral mediator for BIA-ALCL to develop. Certainly particle shedding and possibly friction are contributors to this inflammatory load.</p> <p>This is important because, in contrast to the implications of the surface area/bacteria hypothesis, patients should retain access to properly constructed PU implants. PU implants offer patients safety benefits not available with any other implant surface. See attached text book chapter and associated references taken from 'Biomaterials in Plastic Surgery: Breast Implants Woodhead Publishing, Cambridge'.</p> <p>The author of this submission is a member of the Australian TGA's Expert Working Group on breast implants which recently cancelled the registration of the only remaining PU implant available in Australia, Polytech.</p> <p>SCHEER should be aware that this decision was based on an assumed class effect for PU implants that ignored the Silimed specific delamination manufacturing fault and an apparently counterfactual determination that PU implants do not offer any benefits compared to other implant surfaces.</p> <p>Consequently, Australian women are now suffering harm from avoidable complications.</p>	
143	Mercer Nigel, Plastic, Reconstructive and Aesthetic Expert Advisory Group (PRASEAG), United Kingdom	6.4. Mediating and/or moderating factors associated with the risk of BIA- ALCL	<p>P32 Line 32: The word 'textured' should be removed.</p> <p>P32 Line 41: A 'subfraction' is not a very user friendly term. It would be better to use the data quoted e.g., "less than xxx people with implants will develop BIA-ALCL"</p> <p>P32 Line 40: Genetic alterations: The difference needs to be made clear between somatic and germline genetic alterations and their roles.</p> <p>P32 Line 53-56: There is little evidence to support this is a huge statement. Without supporting evidence, such suppositions/hypothesis presented as a statement from a responsible body are dangerous! A statement that, 'causal links between germline cancer predisposition mutations and BIA-ALCL risks are being explored' It is unscientific to go</p>	<p>P32 line 32. SCHEER disagrees in all but one of the BIA-ALCL cases where the implant history is known are associated with the presence of an implant with a textured surface. SCHEER has modified the conclusion on textured in the Abstract, Conclusion and answer to Q5.</p> <p>""Overall SCHEER considers that there is a moderate weight of evidence for a causal relationship between textured breast implants and BIA-ALCL, particularly in relation to implants with an intermediate to high surface roughness.</p> <p>At this point it should be noted that i) there are several types of textured implants ii) surface textures of breast implants are not all manufactured in the same way, and iii) implants with diverse surface</p>

			<p>further with out evidence.</p> <p>P33 Line 3: De Boer et al published 2020 is not in their reference list the correct reference is.... 'Increased prevalence of BRCA1/2 mutations in women with macrot textured breast implants and anaplastic large cell lymphoma of the breast (<a href="https://doi.org/10.1182/blood.2019004498">https://doi.org/10.1182/blood.2019004498</a> ). This link does not work The letter cannot be accessed. It appears not to be peer reviewed and, therefore, has to be interpreted with caution</p> <p>P35 Line 12: Conclusions Are germline or somatic DNA mutations being referred to?</p>	<p>textures may also present different benefits. The magnitude of the risk per type of textured implant is difficult to establish due to the low incidence of the risk. Even with macro-textured implants, BIA-ALCL has a very low incidence. Therefore, risk assessments per implant type are needed. Furthermore, the risk should be weighed against the benefits. There is also a need for an unambiguous, clinically validated classification system for breast implants including more parameters than just “surface roughness”. A history of textured breast implants/expanders appears to be necessary but not sufficient for the development of BIA-ALCL.”</p> <p>P32 line 41. SCHEER agrees. Text changed to “very minor group”</p> <p>P32 line53-56. SCHEER disagrees. The issue is mentioned including a warning that these are very preliminary results.</p> <p>“In all, these studies have been conducted with limited numbers of patients and require expansion with far larger cohorts before conclusions can be made.”</p> <p>Reference De Boer et al 2020 has been added to the reference list.</p> <p>P35 line12. Local mutations in cells near the breast implant i.e. somatic are meant here as mutations that might be due to toxic metabolites originating from the implant.</p> <p>The text has been adapted: “Alternatively, additively, gene mutations might also be a consequence of exposure to aryl hydrocarbons whereby toxic metabolites induce transversions in the genetic code of cells in the vicinity of the implant.”</p>
144	Mercer Nigel, Plastic, Reconstructive and Aesthetic Surgery Expert	6.4. Mediating and/or moderatin g factors	<p>P32 Line 32: The word ‘textured’ should be removed.</p> <p>P32 Line 41: A ‘subfraction’ is not a very user friendly term. It would be better to use the data quoted e.g., “less than xxx people with implants will develop BIA-ALCL”</p>	<p>P32 line 32. SCHEER disagrees in all but one BIA-ALCL case of which the implant history is known, are associated with the presence of an implant with a textured surface. SCHEER has modified the conclusion on textured in the Abstract, Conclusion and answer to Q5.</p>

	Advisory Group (PRASEAG), United Kingdom	associated with the risk of BIA-ALCL	<p>P32 Line 40: Genetic alterations: The difference needs to be made clear between somatic and germline genetic alterations and their roles.</p> <p>P32 Line 53-56: There is little evidence to support this is a huge statement. Without supporting evidence, such suppositions/hypothesis presented as a statement from a responsible body are dangerous! A statement that, 'causal links between germline cancer predisposition mutations and BIA-ALCL risks are being explored' It is unscientific to go further with out evidence.</p> <p>P33 Line 3: De Boer et al published 2020 is not in their reference list the correct reference is.... 'Increased prevalence of BRCA1/2 mutations in women with macrot textured breast implants and anaplastic large cell lymphoma of the breast (<a href="https://doi.org/10.1182/blood.2019004498">https://doi.org/10.1182/blood.2019004498</a>)'. This link does not work The letter cannot be accessed. It appears not to be peer reviewed and, therefore, has to be interpreted with caution</p>	<p>“Overall SCHEER considers that there is a moderate weight of evidence for a causal relationship between textured breast implants and BIA-ALCL, particularly in relation to implants with an intermediate to high surface roughness.</p> <p>At this point it should be noted that i) there are several types of textured implants ii) surface textures of breast implants are not all manufactured in the same way, and iii) implants with diverse surface textures may also present different benefits. The magnitude of the risk per type of textured implant is difficult to establish due to the low incidence of the risk. Even with macro-textured implants, BIA-ALCL has a very low incidence. Therefore, risk assessments per implant type are needed. Furthermore, the risk should be weighed against the benefits. There is also a need for an unambiguous, clinically validated classification system for breast implants including more parameters than just “surface roughness”. A history of textured breast implants/expanders appears to be necessary but not sufficient for the development of BIA-ALCL.”</p> <p>P32line 41. SCHEER agrees. Text changed to “very minor group”</p> <p>P32line53-56. SCHEER disagrees. The issue is mentioned, including a warning that these are very preliminary results.</p> <p>“In all, these studies have been conducted with limited numbers of patients and require expansion with far larger cohorts before conclusions can be made.”</p> <p>Reference De Boer et al 2020 is added to the reference list.</p>
145	Geertsma Robert, RIVM - National Institute for Public Health and the Environment	6.5 The safety of breast implants in relation to	6.5 lines 35-37 Again: not all textured implants have the same risk profile. In addition: here, the importance of benefit-risk of different type of implants is correctly mentioned. This should be done throughout the Opinion (see	New text has been prepared for the Abstract, Conclusion, and answer to Q5.

		BIA-ALCL	also previous comments).	<p>““Based on these data, SCHEER considers that there is a moderate weight of evidence for a causal relationship between textured breast implants and BIA-ALCL, particularly in relation to implants with an intermediate to high surface roughness.</p> <p>At this point it should be noted that i) there are several types of textured implants ii) surface textures of breast implants are not all manufactured in the same way, and iii) implants with diverse surface textures may also present different benefits. The magnitude of the risk per type of textured implant is difficult to establish due to the low incidence of the risk. Even with macro-textured implants, BIA-ALCL has a very low incidence. Therefore, risk assessments per implant type are needed. Furthermore, the risk should be weighed against the benefits. There is also a need for an unambiguous, clinically validated classification system for breast implants including more parameters than just “surface roughness”. A history of textured breast implants/expanders appears to be necessary but not sufficient for the development of BIA-ALCL.”</p>
146	MELVIN Tom, HPRA, Ireland	6.5 The safety of breast implants in relation to BIA-ALCL	<p>General comment Could the SCHEER account for different levels of awareness of patients, family doctors, breast clinics, radiologists, histopathologists and cosmetic surgeons when considering risk control measures?</p> <p>Has the SCHEER considered feedback from patient groups or representatives regarding this?</p> <p>Awareness of BIA-ALCL is vital when the risk control measures suggested in the opinion involve vigilance of patients and healthcare practitioners, and consideration of relative risks with different products.</p>	<p>SCHEER has only evaluated the scientific evidence for the relationship between breast implants and BIA-ALCL.</p> <p>Evaluation of the awareness of various involved groups has not been considered. However, it became clear that the rise in awareness amongst professionals treating BIA-ALCL has added substantially to the increase in diagnosis of BIA-ALCL.</p>
147	Brotherston Chris, GC Aesthetics, Ireland	6.5 The safety of breast implants in relation to	All breast implants regardless of surface texture are associated with risks, especially considering the nature of the procedure and the number of factors involved in a successful surgery. Textured implants may be associated with a higher risk of ALCL, but they also offer lower incidences of capsular contracture, malposition and rotation (which are	SCHEER agrees with the comments, and has also emphasized the different benefits of the various types of implants.

	<p>BIA-ALCL</p> <p>common complications) in comparison to other surfaces (Liu et al, 2015).</p>  <p>GC_Aesthetics_Scheer_Point_6.5_4_Dec_20</p> <p>Calobrace et al (2018) performed a 20 year review on the long term safety and efficacy of textured implants using data from the three Core Studies approved by the FDA from Allergan, Mentor and Sientra. They found ‘the importance of maintaining [smooth and textured breast implants] to assess the risks and benefits of the choices to provide the best individual outcome for each patient’. Calobrace et al (2018) also explains how textured implants reduce the incidence of capsular contracture and balances this with more recent literature outlining the complications with textured implants and BIA-ALCL and states that different implant textures ‘perform different clinically, and many of the benefits and risks associated with textured surfaces are specific to each surface texture’. Calobrace et al (2018) concluded that the stability of textured implants in the breast pocket may support better outcomes in patients with</p> <ul style="list-style-type: none"> <li>• chest wall abnormalities,</li> <li>• revision breast cases,</li> <li>• poor soft tissue cases including mastopexies,</li> <li>• And that textured implants may reduce risk for capsular contracture in all cases.</li> <li>• Texture also provides the pocket control and position stability for shaped implants utilized in appropriate aesthetic or reconstructive cases.</li> </ul> <p>There are a number of other papers citing benefits of textured implants which need to be taken into consideration. For example: Danilla et al (2020) has recently conducted an economic analysis of the costs that banning textured would have and found that if this was utilized in a preventative measure against BIA-ALCL it would not be cost effective. Furthermore they have modeled the consequences such as</p>	<p>Text has been added:</p> <p>“At this point it should be noted that i) there are several types of textured implants ii) surface textures of breast implants are not all manufactured in the same way, and iii) implants with diverse surface textures may also present different benefits. The magnitude of the risk per type of textured implant is difficult to establish due to the low incidence of the risk. Even with macro-textured implants, BIA-ALCL has a very low incidence. Therefore, risk assessments per implant type are needed. Furthermore, the risk should be weighed against the benefits. There is also a need for an unambiguous, clinically validated classification system for breast implants including more parameters than just “surface roughness”. Text of section 6.5 has been adapted:</p> <p>“Breast implants carry a reasonable assurance of safety and efficacy in that they perform as they were intended as indicated by the long term follow-up evaluated by Calobrace et al. (Calobrace et al. 2018).”</p> <p>The mandate for this Opinion was to provide an evaluation of the risk of BIA-ALCL in regard to breast implants. Therefore, it is out of the scope of this Opinion to include all benefits and/or risk of all the types of implants on the market worldwide.</p>
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			<p>the mortality and morbidity sequelae resulting from an increase of capsular contraction rates with associated increase of reoperation rates which need to be weighed against the potential reduced rates of BIA-ALCL.</p> <p>Atlan et al (2018) looked at the textured surfaces and found that with textured implants there was better tissue growth which disrupted the capsule fibre organization and increases the tissue adherence which could lead to a reduction of capsular contraction or malpositioning.</p> <p>Many competent authorities continue to recognise the benefits of textured breast implants and as such recommend physicians to discuss the benefits and risks with their patient prior to making a decision on implant type. Breast augmentation is still the most frequently performed aesthetic surgical procedure worldwide. Therefore, it is perceived to provide significant benefits for a substantial patient group. Bearing this in mind extreme care should be taken in limiting the use of textured implants as a control measure as this is linked to other concomitant clinical outcomes as described above.</p> <p>GC Aesthetics has an excellent safety profile and takes all the necessary steps to ensure that all risks associated with the textured implants are minimized by applying the available state-of-the-art techniques to their design and manufacture. In addition, GC Aesthetics is committed to adequately providing surgeons and patients with the most up to date information on risks and benefits of all our implants in order for them to make a fully informed choice.</p> <p>References provided.</p>	
148	Parreira Carlos, EASAPS ESAPS, Belgium	6.5 The safety of breast implants in relation to BIA-ALCL	<p>Line 25-7:  “However, and based on epidemiological and other data from Competent Authorities, the lifetime incidence of BIA-ALCL has increased dramatically from initial reports of 1 per million to current overall estimates of approximately 1 per 3000 women in Australia and the Netherlands.”</p>	<p>The text has been modified:</p> <p>“However, and based on epidemiological and other data from Competent Authorities, the lifetime incidence of BIA-ALCL has increased dramatically from initial reports of 1 per million to current</p>

			<p>Although, the incidence has raised dramatically in Australia and the Netherlands this is not true for the majority of the European countries. So this sentence should be more careful:  “However, and based on epidemiological and other data from Competent Authorities, the estimation of the lifetime incidence of BIA-ALCL in women with implants has increased significantly over the last years. Initial reports state 1 per million, and now in two countries (Australia and the Netherlands) it has increased to 1 per 3000 women.”</p>	<p>highest estimates of approximately 1 per 3000 women with a breast implant in Australia and the Netherlands.”</p>
149	Cristian Radu Jecan, Romanian Association of Plastic Surgeons, Romania	6.5 The safety of breast implants in relation to BIA-ALCL	<p>Page 35 - lines 20-52. RoAPS support E(A)SAPS comment that the collaborators of the SCHEER report must be commended for their efforts to describe the relation between ALCL and breast implants. It is regrettable however that the viewpoints of aesthetic plastic surgeons is not taken sufficiently into account. Epidemiology and incidence rates for BIA-ALCL should not be exclusively based on two populations. Manufacturers should provide information on European sales data during the last 10 years. Reporting BIA-ALCL cases should be mandatory for all clinical institutions. Up and running breast implant registries should capture these cases. Consensus guidelines for patients with textured implants who wish to remove them are needed. A central European laboratory with main focus on future research with respect to BIA-ALCL histopathology and genetics is recommended. E(A)SAPS is always willing to collaborate and demands for an urgent revision taking the above remarks into account.</p>	<p>All professional groups involved had the possibility to provide information for the content of this Opinion. Besides the Public Consultation there was also a call for participation and information. (<a href="https://ec.europa.eu/health/scientific_committees/call_experts/call_experts_bia_alcl_en">https://ec.europa.eu/health/scientific_committees/call_experts/call_experts_bia_alcl_en</a>), the deadline of which was actually extended once (from December 4th, 2019 to January 3rd, 2020) due to the low response received from experts.</p>
150	Mercer Nigel, Plastic, Reconstructive and Aesthetic Expert Advisory Group (PRASEAG), United Kingdom	6.5 The safety of breast implants in relation to BIA-ALCL	<p>P35 line 22: ‘reasonable assurance of safety and efficacy’ ... This needs qualification. By what and by whose definition ?</p> <p>P35 Line 23-24: In the same way, how reasonable is it to state the majority of patients are happy with breast implants? It seems a reasonable statement on the face of it but evidence should be quoted because this is an evidence based paper.</p> <p>P35 Line 25-28: Can it be stated that the lifetime incidence has increased dramatically when the disease was not recognised until 2016 and figures prior to 2016 will, therefore, be inaccurate.</p> <p>P35 L36: low absolute but high relative risk: This has been mentioned</p>	<p>P35 line 22 Reference added.</p> <p>“Breast implants carry a reasonable assurance of safety and efficacy in that they perform as they were intended as indicated by the long term follow-up evaluated by Calobrace et al. (Calobrace et al. 2018).”</p> <p>P35 line 23-24. Patient satisfaction has been addressed above</p> <p>References added. Ng et al. 2019, Kouwenberg et al. 2020. P35 line 25-28. SCHEER disagrees on date of 2016 as the date of recognition of BIA-ALCL. It was recognised by plastic surgeons before 2016.</p>


			<p>this before (P30 L 21) but we are encouraged not to use relative risk when counselling patients because it tends to inflate the impact of the numbers on a lay person. Please provide a more clinically informative and patient friendly term?</p>	<p>However, it is indicated in the Opinion that figures are not fully reliable in view of the lack of information on the number of women with breast implants (i.e. the denominator).</p> <p>Also, it is mentioned in the Opinion that certainly the rise in awareness amongst professionals dealing with breast implants contributed to the increase in incidence. Also the description of clear diagnostic criteria will have contributed to an increase in cases over the years.</p> <p>P35 line36 (and P30 line20) indicates a relative risk. SCHEER disagrees that relative risk is not important. Most data give the relative risk a one case per X patients, the highest being 1 in approximately 3000 as observed in the Netherlands and Australia. Cordeiro et al. 2020 indicates in a study 1 in 355 in a specific group of patients. A follow up study on this study was reported by Nelson et al. 2020. Text modified to include follow up study of Nelson et al. 2020. Also the denominator is different in each case, e.g. women with any implant, women with Biocell implants, etc.</p> <p>Text added.</p> <p>“ This study was extended to include 9373 patients over the period 1991-2017, of which eleven women developed BIA-ALCL all with a history of textured implants. The 26-year incidence of BIA-ALCL was reported as 1 in 559 patients and 1 in 871 textured implants (0.11%) (Nelson et al., 2020).”</p>
151	Decaluwé Kelly, Federal Agency of Medicines and Health Products, Belgium	6.5 The safety of breast implants in relation to BIA-ALCL	<p>Line 22 - 23 In section 2.1 Answers to the Terms of References (line 10-13) it was stated that an appropriate control measure to reduce the identified risk (being BIA-ALCL) is to limit the use of textured implants. In section 6.5 however you state that breast implants (also textured implants) carry a reasonable assurance of safety and efficacy. This might be perceived as contradictory and therefore the FAMHP suggests the experts to elaborate on this. It should, in our opinion, be clarified that the benefit/risk balance should not be limited to BIA-ALCL but rather needs to take into account all risks. In that perspective, it is of great</p>	<p>Reference added:</p> <p>“Breast implants carry a reasonable assurance of safety and efficacy in that they perform as they were intended as indicated by the long term follow-up evaluated by Calobrace et al. (Calobrace et al. 2018).</p>

			<p>importance to consider whether reduction of BIA-ALCL risk by limiting the use of textured implants would significant shift the risk profile of breast implants (e.g. increased rates of revisions due to capsular contracture). Registries and comparative studies are important tools to study this and may help in the determination of advantages/disadvantages for the different options in specific patient groups. Also patient education with emphasizes on the well-informed decision making process could be considered as risk control measures. However, a better estimation of the risks and better knowledge on advantages/disadvantages for the different options are needed to improve patient education in order for the patient to really make a well-informed decision.</p>	
152	CAMPANALE ANTONELLA, ITALIAN MINISTRY OF HEALTH, Italy	6.5 The safety of breast implants in relation to BIA-ALCL	<p>p. 35 line 24-27: Although there has been an increase in the number of cases, thanks to the raised awareness and to all the actions undertaken at National level, we believe that the monitoring incidence rate per year is fundamental. In our experience where the method used to estimate the incidence is homogeneous, we observed that although small oscillations were observed between 2015 and 2018, these are not statistically significant, and the disease remains a rare disorder with an incidence of about 3/100.000 implanted patients per year (please read, cite and comment the “The Crucial Role of Surgical Treatment in BIA-ALCL Prognosis in Early- and Advanced-Stage Patients. Campanale A, Spagnoli A, Lispi L, Boldrini R, Marletta M. Plast Reconstr Surg. 2020 Nov;146(5):530e-538e. Online first since August 2020)</p> <p>p.35 line 36-37: Taking into account the lack of data in BIA-ALCL research and the need for an in-depth understanding of the pathophysiology, we disagree with the message that only textured breast implants have to be considered associated in a causal relationship with this disease.</p> <p>BIA-ALCL has been added to the risks of this type of implant surgery and awareness must be constantly promoted for both physicians and patients. We would like to remark that, to date, it still needs to be clarified: - The device implanted at the time of the onset of the first symptoms (recovering a complete and well documented implant history;</p>	<p>SCHEER thanks Dr Campanale for the comment.</p> <p>P35 line 36-37 As indicated in the Opinion SCHEER recognises that there is a relationship between textured surface implants and BIA-ALCL. SCHEER also now indicates the various types of surface textures available and their possible benefits.</p> <p>Text has been modified:</p> <p>“Based on these data, SCHEER considers that there is a moderate weight of evidence for a causal relationship between textured breast implants and BIA-ALCL, particularly in relation to implants with an intermediate to high surface roughness.</p> <p>At this point it should be noted that i) there are several types of textured implants ii) surface textures of breast implants are not all manufactured in the same way, and iii) implants with diverse surface textures may also present different benefits. The magnitude of the risk per type of textured implant is difficult to establish due to the low incidence of the risk. Even with macro-textured implants, BIA-ALCL has a very low incidence. Therefore, risk assessments per implant type are needed. Furthermore, the risk should be weighed against the benefits. There is also a need for an unambiguous, clinically validated</p>


			<ul style="list-style-type: none"> <li>- Why with the same device, only very few patients develop this disease,</li> <li>- The role of genetic factors (genetic predisposition)</li> </ul>	<p>classification system for breast implants including more parameters than just “surface roughness”. A history of textured breast implants/expanders appears to be necessary but not sufficient for the development of BIA-ALCL.”</p>
153	Kerr Lisa, Therapeutic Goods Administration, Australia	6.6 Future directions/ research	<p>We agree that there is an imminent need for an in-depth understanding of the pathophysiology and the role of patient genetics and/or the microbiome as well as features of the implant devices themselves in the development of BIA-ALCL.</p> <p>In addition to the post-market review of breast implants in Australia (including laboratory assessment of surface topography and the statistical analysis of breast implant supply with known cases of BIA-ALCL), the TGA has put together a consultation paper, working together with the International working group (IWG) on breast implant surface texture classification, including members of the International Collaboration of Breast Device Registry Activities (ICOBRA), and the Regulatory agencies from Europe, Australia, Canada and the US, to amend ISO 14607 (WG 8), as there is a need for a more specific surface texture classification as to enable a surface specific benefit-risk assessment in the market authorisation system.</p> <p>Specifically, amendments to the ISO Standard proposed are the following:</p> <ul style="list-style-type: none"> <li>• To introduce an implant classification scheme that uses a multipolar system to include production method, average surface roughness and surface area ratio.</li> <li>• To include the following parameters as a mandatory part of the Standard: <ul style="list-style-type: none"> <li>- That under ISO 10993-1, all endpoints of biological evaluation are assessed for mammary implants. Implantation studies under ISO 10993-6 undertaken using adequate controls, with appropriately scaled versions of actual textured devices used to meaningfully evaluate the effect of texturing; moreover, the implantation site has to be relevant for the intended use of the device.</li> <li>- That implantation studies are undertaken for a period exceeding 12</li> </ul> </li> </ul>	<p>SCHEER thanks Dr Kerr for these comments. The TGA report on breast implant surfaces is included in section 4.6 Breast implants surfaces. Also, the revision of ISO 14607:2018 is mentioned in 4.6.</p> <p>In 6.6, SCHEER has added text to emphasise the role of implant surface.</p> <p>“There is a need to further evaluate the role of the implant surface on the induction of BIA-ALCL. For a proper characterization and classification of the implants surface, more in depth knowledge of the surface is needed beyond average surface roughness.”</p>

			<p>weeks to appropriately reflect the duration of implantation.</p> <ul style="list-style-type: none"> <li>• To include the evaluation of particulate contamination on implant surfaces</li> </ul>	
154	Brotherston Chris, GC Aesthetics, Ireland	6.6 Future directions/research	<p>For the Attention of the SCHEER Committee Please find our response to Point 6.6</p>  <p>SCHEER_point_6.6.pdf</p> <p>Point 6.6 GC Aesthetics agree that there is a need for further in-depth research into BIA-ALCL as it is such a new and emerging disease. Large scale studies are needed to understand the link between BIA-ALCL and textured mammary implants as recent publications suggest a multifactorial cause of the disease. GC Aesthetics would share sales data with appropriately controlled organisation under confidentiality to further this research but we believe registries give best indicators of the number of implantations. We believe that with standardisation of texture classification, mandatory registries and mandatory reporting to competent authorities, the true data and causal links will be better understood.</p> <p>We recognise and agree that mandatory registries would be beneficial so that true case numbers are known and that as stakeholders we should collaborate closely with regulatory bodies and our customers as suggested by Kim et al (2020)</p> <p>We recognise that industry also needs closer links in the research space into BIA-ALCL in a non-commercial and transparent manner.</p> <p>References Kim J H , Paik N-S , NamSY ,Cho Y, Park HK. The Emerging Crisis of Stakeholders in Implant-based Augmentation Mammoplasty in Korea. J Korean Med Sci. 2020 Apr 20;35(15):e103</p>	<p>SCHEER thanks Dr Brotherston for the comment and the offer to share sales data.</p>
155	AYHAN SUHAN, GAZI UNIVERSITY	6.6 Future directions/	<p>At this point, I have to argue with the comment of SCHEER that “the clinical indications of the use of a specific type of breast implant does</p>	

	FACULTY OF MEDICINE, TURKEY	research	<p>not depend on the clinical conditions but only on the clinician’s and patient’s preference and consequently on industry and/or media information”, which is not true. We must put it in a right way: In good clinical practice, surgeons see their patients, examine and measure their patients, talk to their patients, assess their needs and preferences and finally select the best suitable and available implants for them. Unethical surgeons who are involved in mass production or under the influence of industry should not be viewed as examples for the ones who are following principles of good clinical practice.</p> <p>Anatomical implants are important tools to achieve natural and long-lasting results after breast reconstruction and augmentation and I would like to emphasize how essential it is for a plastic surgeon to have a variety of breast implants. At the end, smooth round implants are associated with other complications such as capsular contracture and a return to smooth implants may cause more additional surgeries, including implant exchange, fat grafting and autologous tissues.</p> <p>This issue should be considered more carefully from a cost-effectiveness and risk-benefit point of view, because the eventual ban of all textured implants will cause trouble in use of anatomical implants. I must stress the fact that surgeons could lose the opportunity to provide their patients the best solution for their health if microtextured and PU implants are banned. If this happens, patients will be deprived of the opportunity of having the implants with least capsular contracture rates and least possibility of rotation, and the chance of receiving cheaper prepectoral breast reconstruction without using any ADM. The clinical advantages and even superiority of PU implants have been confirmed in several clinical and research studies. 10-14</p> <p>In conclusion,</p> <ul style="list-style-type: none"> <li>• BIA-ALCL is an extremely rare disease. Any implant can be associated with the BIA-ALCL, but the most important actor is withdrawn and out of the market now. It is for sure that surgeons have to be alert at all times. We have to inform our patients, call them for regular follow-ups, educate them for symptoms and test all late seromas.</li> <li>• The data in the literature is not conclusive and we definitely need</li> </ul>	<p>The text on implant choice has been modified:</p> <p>““Some trends are apparent in the literature for the use of one or another type of breast implant. However, the clinical indications for the use of a specific type of breast implant should depend on a consultation between clinician and patient to allow informed decision making to take place with regards to the choice of an appropriate breast implant. For breast reconstruction a shared consultation with a multidisciplinary healthcare team including a pathologist, oncologist, surgeon, breast care nurse, etc should be held with the patient to allow informed decision making to take place with regards to the breast reconstruction procedure as well as the choice of implant. For both aesthetic and reconstructive surgery all aspects of breast implants should be evaluated and discussed with the patient, expressly covering advantages, disadvantages, follow-up procedures and risk factors.”</p> <p>The text on the causal relationship has been modified to indicate the multiple forms of surface textures.</p> <p>“Based on these data, SCHEER considers that there is a moderate weight of evidence for a causal relationship between textured breast implants and BIA-ALCL, particularly in relation to implants with an intermediate to high surface roughness.</p> <p>At this point it should be noted that i) there are several types of textured implants ii) surface textures of breast implants are not all manufactured in the same way, and iii) implants with diverse surface textures may also present different benefits. The magnitude of the risk per type of textured implant is difficult to establish due to the low incidence of the risk. Even with macro-textured implants, BIA-ALCL has a very low incidence. Therefore, risk assessments per implant type are needed. Furthermore, the risk should be weighed against the</p>
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			<p>prospective and randomized studies before deciding for a ban of a wide spectrum of implants.</p> <ul style="list-style-type: none"> <li>• In good clinical practice, implant selection is based on the patient’s characteristics and the experience of the surgeon. We need implants and we need not only smooth and round implants but anatomical implants as well. If we can only use smooth implants, it is not going to be a surprise to expect high number of complications in the future as it was reported in the past.</li> <li>• Macrot textured implants should be avoided, but micro textured implants should NOT be banned. Polyurethane implants are NOT macrot textured implants. Whenever polyurethane implants are indicated, the benefit exceeds the risk by far.</li> <li>• Eradication of macrot textured implants from the market are sufficient by now and there is no need for additional ban. However, implant registry is the most essential move for the safety of our patients in the future.</li> </ul> <p> SCHEER-comment-MSA.pdf</p>	<p>benefits. There is also a need for an unambiguous, clinically validated classification system for breast implants including more parameters than just “surface roughness”. A history of textured breast implants/expanders appears to be necessary but not sufficient for the development of BIA-ALCL.”</p> <p>Regarding polyurethane implants, the text has been modified in section 6.2 Conclusions:</p> <p>“As far as the manufacturer for textured implants was known, most cases were found for the Biocell implant (texture by salt loss technique), while for PU coated breast implants BIA-ALCL cases were mainly associated with the Silimed implant. Cases for other manufacturers were much lower. Although they cannot be considered to induce a textured surface on an implant, PU coating does result in an increase in surface area and roughness. For the PU coated Silimed implants, the highest surface roughness and surface area was observed when various brands of breast implants were compared with each other (Jones et al. 2018).”</p>
156	Mercer Nigel, Plastic, Reconstructive and Aesthetic Expert Advisory Group (PRASEAG), United Kingdom	6.6 Future directions/ research	P35 Line 42: patient genetics: To what does this refer? Patient (germline) and BIA-ALCL (somatic) genetics?	As indicated in section 6.4, both gene alterations were reported in the germ-line cell as well as in the tumour cells themselves. Since this was reported in only a small number of cases, more research in this area is needed, as stated in section 6.6.
157	CAMPANALE ANTONELLA, ITALIAN MINISTRY OF HEALTH, Italy	6.6 Future directions/ research	p.35 line 39: We do believe that the following comments should be considered for this section: - Mandatory breast implant registries have to be promoted and supported with a common minimum data set that makes the data collected comparable - Pre-market studies have to be enhanced as well as the classification of	Section 6.6 indicates general aspects of directions for possible future research. More specific recommendations are presented in section 2.1 in the answer to Question 8 of the mandate.  Text has been modified to clearly indicate this aspect.  “As BIA-ALCL is an uncommon malignancy, finding answers needs



			<p>breast implant surfaces (an international TF is already at work on this matter)</p> <ul style="list-style-type: none"> <li>- Considering the improvements given by these devices to the quality of life of 35 millions of women worldwide, corrective action against textured breast implants cannot be supported.</li> <li>- Genetic studies have to be supported in order to understand why with the same device only very few patients develop this disease</li> </ul>	<p>further research as presented above in section 2.1 “Answers to the Terms of References”.</p>
158	Parreira Carlos, EASAPS ESAPS, Belgium	8. REFERENC ES	<p>Trente-six cas français de lymphomes anaplasiques à grandes cellules associés aux implants mammaires. Que savons-nous sur leur histoire prothétique ? Thirty-six (36) French cases of Breast Implant-Associated Anaplastic Large Cell Lymphoma (BIA-ALCL): What do we know about their prosthetic histories, and what conclusions may be drawn?</p> <p> SCHEER_2nd_submission_1.2.docx</p> <p>L.RuffenachC.Bruant-RodierF.GoldammerE.RamelliF.BodinC.Dissaux Annales de Chirurgie Plastique Esthétique, Volume 64, Issue 4, August 2019, Pages 285-292 Doi : 10.1016/j.anplas.2019.05.002</p>	<p>The text on alternatives for aesthetic patients has been modified.</p> <p>Answer to Q7 : “ There are several alternatives to breast implants that involve plastic surgery techniques, either using autologous flap tissue or autologous fat transfer. The latter may need multiple procedures before an acceptable result is obtained. However, patient characteristics may limit the application of these techniques, and , these techniques are rarely used outside of reconstructive surgery. “</p> <p>Section 4.3 Alternatives text added:</p> <p>“However, the predictability of outcomes with autologous fat transfer may be uncertain, especially in cases in which radiotherapy was applied. Also, patients have to undergo several operative sessions for aesthetic purposes. Moreover, repetitive fat graft sessions might not be possible in some patients because of a lack of availability of the required fat volume (e.g. a slim body with a low Body Mass Index).</p> <p>Fat transfer can be combined with a non-surgical external expansion by sustained tension (generated by a low negative pressure) on the natural breast tissue to cause the cells to proliferate (Oranges et al., 2018). “</p>

			<p>Regarding the lack of involvement of ASSAPS/ESAPS plastic surgeons.:</p> <p>All professional groups have had the opportunity to provide information for the content of this Opinion. Besides the Public Consultation there was a call for participation and information.</p> <p>There was a public, open call for experts to participate and to submit information in the respective working group formed by SCHEER (<a href="https://ec.europa.eu/health/scientific_committees/call_experts/call_experts_bia_alcl_en">https://ec.europa.eu/health/scientific_committees/call_experts/call_experts_bia_alcl_en</a>), the deadline of which was actually extended once (from December 4th, 2019 to January 3rd, 2020) due to the low response received from experts.</p> <p>The text on textured implants has been modified:</p> <p>“Based on these data, SCHEER considers that there is a moderate weight of evidence for a causal relationship between textured breast implants and BIA-ALCL, particularly in relation to implants with an intermediate to high surface roughness.</p> <p>At this point it should be noted that i) there are several types of textured implants ii) surface textures of breast implants are not all manufactured in the same way, and iii) implants with diverse surface textures may also present different benefits. The magnitude of the risk per type of textured implant is difficult to establish due to the low incidence of the risk. Even with macro-textured implants, BIA-ALCL has a very low incidence. Therefore, risk assessments per implant type are needed. Furthermore, the risk should be weighed against the benefits. There is also a need for an unambiguous, clinically validated classification system for breast implants including more parameters than just “surface roughness”. A history of textured breast implants/expanders appears to be necessary but not sufficient for the development of BIA-ALCL.”</p> <p>The text on implants choice has been modified:</p>
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				<p>““Some trends are apparent in the literature for the use of one or another type of breast implant. However, the clinical indications for the use of a specific type of breast implant should depend on a consultation between clinician and patient to allow informed decision making to take place with regards to the choice of an appropriate breast implant. For breast reconstruction a shared consultation with a multidisciplinary healthcare team including a pathologist, oncologist, surgeon, breast care nurse, etc. should be held with the patient to allow informed decision making to take place with regards to the breast reconstruction procedure as well as the choice of implant. For both aesthetic and reconstructive surgery all aspects of breast implants should be evaluated and discussed with the patient, expressly covering advantages, disadvantages, follow-up procedures and risk factors.”</p> <p>Section 6.3 text modified and Ruffenach et al. 2019 cited:</p> <p>“Ruffenach et al. (2019) evaluated 36 cases in the LYMPHOPATH registry and reported that all 36 patients with BIA-ALCL had either a macro-textured implant manufactured with the Biocell salt loss technique or a history of a macro-textured implant.”</p> <p>The text on incidence for two countries has been adapted.</p> <p>“The estimation of the lifetime incidence of BIA-ALCL in women with implants has increased as presented in initial reports from 1 per million to current highest estimates of approximately 1 per 3000 women in Australia and the Netherlands.”</p> <p>Based on epidemiology, the text of the conclusion in section 6.2 was expanded:</p> <p>“As far as the manufacturer for textured implants was known most cases were found in the context of Biocell implants (texture manufactured by salt loss technique), while for PU coated breast implants, BIA-ALCL cases were mainly associated with the Silimed</p>
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				<p>implant. Cases for other manufacturers were much lower. Although it cannot be considered to induce a textured surface on an implant, PU coating does result in an increase in surface area and roughness. The highest surface roughness and surface area was observed for PU coated Silimed implants, when various brands of breast implants were compared with each other (Jones et al. 2018).”</p> <p>Section 2.1.5 The text has been modified.</p> <p>“However, some patients may request removal of the implant and capsule, particularly patients with manufacturer-recalled implants or the reported high-risk breast implants (e.g. certain polyurethane, salt-loss macrotextured, etc.).”</p> <p>Section 2.1.6 The text on risk reduction has been modified:</p> <p>“The full aetiology is not yet understood, although an appropriate control measure to reduce the identified risk is to limit the use of macro-textured implants, notably those prepared by the salt loss technique, and a certain type of PU coating.”</p> <p>Section 2.1.7 The text on alternatives to breast implants has been modified:</p> <p>“The latter may need multiple procedures before an acceptable result is obtained. However, patient characteristics may limit the application of these techniques which are rarely used outside of reconstructive surgery.”</p> <p>And in 4.3 d. See above.</p>
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159	AYHAN SUHAN, GAZI UNIVERSITY FACULTY OF MEDICINE, TURKEY	8. REFERENC ES	<p>REFERENCES:</p> <ol style="list-style-type: none"> <li>1. Anna Loch-Wilkinson , et al, Breast Implant-Associated Anaplastic Large Cell Lymphoma in Australia: A Longitudinal Study of Implant and Other Related Risk Factors. <i>Aesthet Surg J.</i> 2019 Nov 18. pii: sjz333. doi: 10.1093/asj/sjz333.</li> <li>2. <a href="https://www.fda.gov/medical-devices/breast-implants/medical-device-reports-breast-implant-associated-anaplastic-large-cell-lymphoma">https://www.fda.gov/medical-devices/breast-implants/medical-device-reports-breast-implant-associated-anaplastic-large-cell-lymphoma</a></li> <li>3. ISO International Organization for Standardization. ISO 1460: 2018— Non-active surgical implants— Mammary implants— Particular requirements. <a href="https://www.iso.org/standard/63973.html">https://www.iso.org/standard/63973.html</a>. Accessed January 7, 2019.</li> <li>4. Atlan et al. Breast implant surface texture impacts host tissue response. <i>J Mech Behav Biomed Mater.</i> 2018 Dec;88:377-385.</li> <li>5. Jones P, Mempin M, Hu H, et al. The functional influence of breast implant outer shell morphology on bacterial attachment and growth. <i>Plast Reconstr Surg.</i> 2018;142:837–849.</li> <li>6. Barr S, et al. Functional biocompatibility testing of silicone breast implants and a novel classification system based on surface roughness. <i>J Mech Behav Biomed Mater.</i> 2017 Nov;75:75-81.</li> <li>7. Loch-Wilkinson A, Beath KJ, Knight RJW, et al.: Breast implant associated anaplastic large cell lymphoma in Australia and New Zealand: High-surface-area textured implants are associated with increased risk. <i>Plast Reconstr Surg</i> 2017; 140: 645–54</li> <li>8. Collett DJ, Rakhorst H, Lennox P, et al.: Current Risk Estimate of Breast Implant– Associated Anaplastic Large Cell Lymphoma in Textured Breast Implants. <i>Plast Reconstr Surg</i> 143: 30S-40S, 2019</li> <li>9. Venhuis, Bastiaan. (2016). Risk analysis of particulate contamination on Silimed silicone-based breast implants.</li> <li>10. Pompei S, Evangelidou D, Arelli F, et al. The modern polyurethane-coated implant in breast augmentation: long-term clinical experience. <i>Aesthetic Surg J</i> 2016;36:1124e9.</li> <li>11. Pompei S, Arelli F, Labardi L, et al. Polyurethane implants in 2-stage breast reconstruction: 9-year clinical experience. <i>Aesthetic Surg J</i> 2017;37:171e6.</li> <li>12. Loreti et al. Immediate Breast Reconstruction after mastectomy with polyurethane implants versus textured implants: A retrospective</li> </ol>	<p>Most of these references are included in the Opinion.</p> <p>Venhuis et al.: this is a report of RIVM on particles and fibers on the surface of the Silimed breast implants. This was the reason for the withdrawal of the EC mark.</p> <p>The paper of Hamdi 2019 is now cited in section 4.6.</p> <p>A number of other papers (Pompei et al, Loreti et al, Manav et al.) deal with capsular contracture and possible benefit of PU implants over textured implants for preventing capsular contracture. As this is not the subject of the Opinion, these papers were not included in the Opinion.</p>
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			<p>study with focus on capsular contracture. The Breast. 54 (2020) 127e132</p> <p>13. Moustapha Hamdi, MD, PhD. Association Between Breast Implant-Associated Anaplastic Large Cell Lymphoma (BIA-ALCL) Risk and Polyurethane Breast Implants: Clinical Evidence and European Perspective Aesthetic Surgery Journal, Volume 39, Issue Supplement_1, March 2019, Pages S49–S54,</p> <p>14. Manav S, Ayhan MS, Deniz E, Özkoçer E, Elmas Ç, Yalinay M, Şahin E. Capsular contracture around silicone miniimplants following bacterial contamination: an in vivo comparative experimental study between textured and polyurethane implants. J Plast Reconstr Aesthet Surg. 2020 Sep;73(9):1747-1757. doi: 10.1016/j.bjps.2020.02.049. Epub 2020 Mar 17.</p>	
160	<p>Vikram Garadi Principal Engineer, Research and Development vgaradi@its.jnj.com Johnson &amp; Johnson</p>	<p>Section 4.2 Section 4.6</p>	<p>Section 4.2 “Types of breast implants”; Line 50-56.</p> <ul style="list-style-type: none"> <li>o The opinion references Gadelmawla et al. 2002 and states that surface texture can be characterized by the following 7 parameters that affect interactions between the implant and host cells. However: <ul style="list-style-type: none"> <li>a) This reference is about general surface metrology, and different parameters and their calculation; it does not reference breast implant or any implant interaction in the body.</li> <li>b) Furthermore, the paper does not define all of the 7 parameters that are being stated (such as pore size or density)</li> </ul> </li> <li>o Would suggest that this paragraph be removed or explicitly state that these 7 parameters are included here because they are in the ISO14607 standard;</li> <li>o There does not appear to be any clinical, pre-clinical, in-vitro or other data to indicate that these 7 parameters are related to implants/host interaction and more important than other surface parameters.</li> </ul> <p>Section 4.6 “Breast Implant surface textures”; Lines 30-37</p> <ul style="list-style-type: none"> <li>o The opinion states that it is recommended to continue use of the ISO14607:2018 surface classification due to wide consensus among scientific and technical communities that deal with breast implants.</li> <li>o While it is the most prevalent, there are serious limitations with this classification system that make it inadequate; therefore, would</li> </ul>	<p>Section 4.2 comment. Text has been modified and ISO 14607:2018 added as reference:  “Surface texture of objects can be characterised by the following features that may affect interactions between the implant and host cells (Gadelmawla et al. 2002, ISO 14607:2018)”:</p> <p>Section 4.6 comment.  Based on comments received and additional information the text in the Answer 4 to the Mandate (section 2.1) has been modified. The limitation of the ISO 14607:2018 is now clearly mentioned, including the current revision of ISO 14607.</p> <p>Section 2.1 Answer 4:  “Surface textures of breast implants are not all manufactured in the same way. Breast implant surface textures are achieved by several different methods, the most commonly used are salt loss, gas diffusion, imprint stamping and polyurethane foam coating. To date,</p>

		<p>recommend that this opinion recognize that the standard is significantly lacking and urge the scientific community to focus on improving the standard and making it more relevant and comparable between manufacturers. The limitations of the current classification include:</p> <p>a) It is based on one factor only, whose measurement can be affected by equipment type, equipment settings, and expertise of the operator. The opinion states earlier (Section 4.2, line 50) that surface texture can be characterized by at least 7 different surface parameters.</p> <p>b) The classifications used in ISO are based on completely arbitrary delineations. It would suggest that an implant that has an average surface roughness of 9.9 is “smooth”, while an implant that has an average surface roughness of 10.0 is “microtextured”.</p> <p>c) Also noteworthy: surface roughness parameter is an “easy” parameter to measure, but there is little evidence to suggest that it is indicative of a clinical outcome. Surface roughness measurement typically started out in a different industry (auto, aerospace, eg) and was primarily applied to machined components with regular spacing/pattern of features as a result of the machining fabrication process. The irregular pattern of all breast implants with a texture is one indication this is not a good parameter</p>	<p>none of the proposed surface texture classifications reported have been validated in a clinical study to determine which classification best predicts the risk of BIA-ALCL.</p> <p>The surface roughness can be described best by using the ISO classification of roughness being: Smooth (&lt;10µm) Micro (10-50µm) or Macro (&gt;50µm) based on the implant average surface roughness (ISO 14607:2018). It should be noted that the ISO 14607:2018 is currently under revision as the classification based on surface roughness only was considered too limited, as was also concluded in the TGA 2019 report.”</p> <p>And section 4.6:</p> <p>“A recent TGA report has evaluated breast implants on the Australian market. (TGA 2019). The TGA concluded that the ISO method did not adequately describe the complexities of surface textures resulting from the myriad of texturing techniques manufacturers employ. Additionally TGA employed micro-Computed Tomography to extend the categories for surface characterization and was able to group breast implants according to surface characteristics. These groupings include polyurethane-coated, closed salt-loss, open salt-loss, imprinting, subsurface gas diffusion, surface gas diffusion and smooth. It was concluded that the current classification systems require refinement and further examination to develop practical and clinical applications.”</p> <p>Section 4.6 conclusions:</p> <p>“The ISO 14607:2018 is currently under revision as the classification based on surface roughness only was considered too limited as was also concluded in the TGA 2019 report.”</p>
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