POLYTECH

Dieburg, October 25th, 2019

Subject: BIA-ALCL – POLYTECH Update October 2019 and Clarification of Misleading Statements

Dear Surgeons, Employees and Partners,

The BIA-ALCL discussion from the outset has been one that has caused division, confusion and in certain cases panic. At POLYTECH, patient safety and surgeon confidence in our products is our *raison d'être*.

At a recent meeting, the so called, *"1st Consensus world conference on BIA ALCL",* a number of statements were made that we wish to discuss and have a right to reply to. As I listened to the speakers at this meeting, I was struck by one thought: We have allowed one uncommon, albeit potentially serious condition, to become the perceived benchmark for safety in our industry.

Per the FDA, in July 2019 there have been 573 cases of BIA-ALCL worldwide, 84% of which are associated with one manufacturer. Thankfully, therefore, very few breast surgeons will ever see a case of BIA-ALCL. We have allowed this condition to define a 'safety debate'. More than this, certain stakeholders, through potentially inappropriate implant choices, are willingly trying to swop one potentially serious but very rare condition for a whole host of complications that have significant, actual and potentially serious consequences.

At POLYTECH, we have always strived to support our surgeons, and in consequence their patients, with transparent and scientific-based information. As a company, we refuse to be drawn into 'point scoring' debates with other manufacturers, that can and do impact negatively our entire industry. We believe that misusing BIA-ALCL as a marketing opportunity is irresponsible.

While there are still many unanswered questions on BIA-ALCL, we believe there is an onus upon all manufacturers, surgeons and interested parties to provide factual and scientific support where it exists, and where information is lacking to invest resources to find answers to those questions.

Below are a series of statements that were made and our responses according to the source-verified, scientific-based information we have at our disposal.

We hope that this document will allow, as it is intended, to dispel certain myths that exist around BIA-ALCL, and to provide surgeons and patients with accurate information with which to help patients make complex decisions and ultimately to select the implant that meets their needs based on facts, not on conjecture.

I will personally welcome any comments that you have on the topics raised below, be they contrary to POLYTECH views or supportive.

I wish you every success and give you my commitment of our support to you, your patients and our specialty.

Sincerely.

Wolfgang Steimel, CEO
POLYTECH Health & Aesthetics GmbH

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BIA-ALCL – POLYTECH UPDATE OCTOBER 2019
AND CLARIFICATION OF MISLEADING STATEMENTS

Summary:

1. The estimated risk of BIA-ALCL, based on the most recent FDA's statistics is between 1:3.000 and 1:30.000 across manufacturers.
2. According to reported and confirmed cases, the risk of BIA-ALCL with POLYTECH Microthane® implants is 1:180.000, which is significantly lower than the 1:3.000-1:30.000 risk ratios published by the FDA.
3. No cases of BIA-ALCL have been associated, to date, with POLYsmoooth® or MESMO® implants.
4. Based on FDA data, it is not possible to claim that there have been no cases of BIA-ALCL associated with smooth breast implants.
5. The higher BIA-ALCL incidence with textured implants has never been denied, considering roundabout 84% of cases of BIA-ALCL worldwide are with Allergan Biocell textured implants. However, the statistical evidence linking implants and ALCL cannot be assumed scientifically as proof of causation in relation to any surface type.
6. Women should attend regular checkups with their doctors – at least once a year. Patients who experience problems, aesthetic impairment or pain following breast implant surgery, should immediately inform their surgeon, and consider the available solutions.
7. According to decades of peer-review literature, the rates of occurrence of capsular contracture, as well as of other complications such as rotation and dislocation, vary in relation to the implant surface[1]:

	Smooth implants	Textured implants	PU-covered implants
Capsular contracture rate	30-50%	15-30%	0-9%

In most of the large studies, the capsular contracture rate for polyurethane-foam-covered implants is as low as 0-3 %.

Recent studies have shown that POLYTECH Microthane® implants are a safe choice for both primary breast augmentation and 2-stage breast reconstruction, and have lower complications even in case of radiation treatment, which is known to dramatically increase the risk of capsular contracture.[2]

[1] Vazquez and Pellon, (2007); Handel, *et al.* (2006); Handel (2006); Handel *et al.* (1991) Kjoller *et al.* (2002); Malata *et al.* (1997) Tebbetts (2001) Szycher and Siciliano (1991).

[2] Pompei *et al.*, (2017); Pompei (2016).

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CLARIFICATION OF MISLEADING STATEMENTS FOLLOWING THE *"1ST CONSENSUS WORLD CONFERENCE ON BIA ALCL"*

MISLEADING STATEMENT	**COMMENTARY AND CLARIFICATION**
The previously held view that BIA ALCL has been reported both for smooth and for Textured implants is not correct and now we know that all cases reported so far, worldwide, have been in patients with Textured implants only.	Multiple, conflicting statements from several sources on the total number of BIA-ALCL cases, and on the absence of cases with smooth implants, have contributed to the current confusion: currently, **it is not possible to assert that BIA-ALCL may not be associated with smooth implants, nor to exclude that cases known today are indeed associated with smooth implants.** In a letter dated February 6th, 2019, addressed to healthcare providers and published on the FDA website, the USA Agency reported that "*while the majority of patients who develop BIA-ALCL have had textured implants, and most cases reported in the literature describe individuals who have had textured implants, there have been reports of BIA-ALCL in patients with smooth-surfaced implants and many reports do not include the surface texture of the implant at the time of diagnosis*"[3]. This was confirmed by Steve Nagel, FDA's spokesperson, on the French CSST hearing in Paris on February 7th. An update as of July 6th, 2019, published on the FDA website[4], reports 26 cases of BIA-ALCL with smooth implants (5% of total cases) and that of these, "*12 have unknown prior history of implants, 7 have a history of textured implants, and 7 have history of prior implants with an unknown texture*".
Apart from one presenter who was promoting Polytech Polyurethane Implants all other experts agreed that we should shift to using smooth Implants in the interest of the patients. I think in his study of 4000 cases of Polytech there were already 2 reported BIA ALCL cases.	No lecturers were promoted by POLYTECH Health & Aesthetics. POLYTECH had no association with and was not a sponsor of this event. To our knowledge, only one invited lecturer is a Microthane user, and was invited by choice of the organization committee. This speaker, a former President of the Belgian Plastic Surgery Society, presented on Polyurethane based on his conviction of the safety and performance of this implant type, as consistently shown by evidence-based medicine. **The 2:4.000 ratio with POLYTECH Microthane mentioned by certain commentators has no basis in fact, and is cause of concern over the misleading and unfair nature of such statements.** Often, the risk with Silimed polyurethane in intentionally, though unscientifically, tied in with the risk with POLYTECH Microthane implants. However, according to reported and confirmed cases, the risk of BIA-ALCL with POLYTECH Microthane® implants is 1:180.000, which is significantly lower than the 1:3.000-1:30.000 risk ratios published by the FDA.

[3] FDA, **"**Breast Implant Associated-Anaplastic Large Cell Lymphoma (BIA-ALCL) - Letter to Health Care Providers**"**, February 6th, 2019. https://www.fda.gov/medical-devices/letters-health-care-providers/breast-implant-associated-anaplastic-large-cell-lymphoma-bia-alcl-letter-health-care-providers

[4] FDA, **"**Medical Device Reports of Breast Implant-Associated Anaplastic Large Cell Lymphoma**"**, July 24th, 2019. https://www.fda.gov/medical-devices/breast-implants/medical-device-reports-breast-implant-associated-anaplastic-large-cell-lymphoma

More and more cases of BIA-ALCL are being identified on a regular basis due to more awareness of the disease. In 2014/15 we were talking on 1:1000,000 then 1:500,00, then 1:100,000 and now we are talking of 1:24,000 in the UK.	Thankfully, it is true that increased awareness and specific testing have led to increased early diagnoses. Early detection leads to timely treatment and in almost all cases to a positive prognosis. The MHRA reported that as of July 2019, it had received 72 reports of ALCL in patients with breast implants, of which 59 meet the official WHO diagnostic criteria for BIA-ALCL. The estimated risk of BIA-ALCL in the UK, based on the reported confirmed cases, is 1 per 24.000 implants sold.[5]
To diagnose one has to actively look out for the disease. Simply waiting for a CD30 positive and ALK negative seroma fluid for diagnosis is not enough.	No authority, medical association or manufacturer ever recommended waiting to develop a large fluid collection as the only possible sign to start the path for the diagnosis and treatment of BIA-ALCL. All serious sources state that the disease is commonly occurring with a seroma (and in this case it needs to be tested by cytology, immunochemistry and flow cytometry) or in alternative/in combination, in fewer cases, with a mass (and in this case the mass requires tissue biopsy and evaluation), or, in even fewer cases, with systemic symptoms. In general, women are always encouraged to perform regular self-checks and attend regular checkups with their doctors – at least once a year. Patients who experience problems, aesthetic impairment or pain following breast implant surgery, should immediately inform their surgeon, and consider the available solutions. That being said, according to the *NCCN Consensus Guidelines 2019*[6], CD30 positive and ALK negative cells in the seroma fluid, still remain the marker to confirm the diagnosis.
A negative cytology can still be associated with BIA-ALCL on careful Wright Giemsa staining and cell block immunohistochemistry of Capsular tissue sent for positive CD30 markers and ALK negative.	According to some sources, in patients with a negative CD 30 cytology who are subsequently diagnosed with BIA-ALCL, the negative cytology result may depend on time or site of testing. In any case, as mentioned, the *NCCN Guidelines 2019*[7] recommend other exams beside cytology, for the proper morphologic examination of the cells.
Seroma is only a presentation in 60 % cases and only 20 % present as pericapsular lump and other 20% can have lumps in deeper gland or in lymph nodes. Some patients without any kind of seroma or lump and with only vague symptoms of pain and discomfort were also diagnosed to be ALCL Positive and some patients initially diagnosed and treated as Breast Cancer were eventually diagnosed as BIA ALCL. So, the conclusion is that more and more cases are being identified by actively looking out for them.	According to Magnusson *et al.* (2019), "*The commonest presentation of BIA-ALCL remains unilateral late seroma, observed in 84 percent of patients*."[8] Also, differential diagnosis is important: mistaken initial diagnosis of BIA-ALCL as breast cancer seem to indicate the lack of awareness of the proper diagnostic tools and guidelines by the involved professionals, as breast cancer is a well-known and in-depth studied entity in all its presentations. Fortunately, the increase in attention on BIA-ALCL is reportedly spreading awareness on the consensus guidelines. Compared to previous times when seroma fluid was never tested for BIA-ALCL, now an increasing number of cases is found and timely treated.

[5] MHRA, "Breast implants and Anaplastic Large Cell Lymphoma (ALCL)", September 26th, 2019.
https://www.gov.uk/guidance/breast-implants-and-anaplastic-large-cell-lymphoma-alcl#mhra-reports

[6] Clemens *et al.* (2019).

[7] Clemens *et al.* (2019).

[8] Magnusson *et al.* (2019).

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<td>While the etiology of BIA ALCL is not yet confirmed and genetic mutations may well be an initiating factor (there's no way at present to identify genetic risk), presence of Biofilm, friction, particles, bacteria and viruses may all play a part. The textured surface provides a perfect source of friction, inflammation, particles and harbouring of Biofilm and bacteria and hence it's not surprising to see that all cases reported so far have been in patients with Textured implants. And as we know from BioCell Allergan and Silimed Polyurethane experience that macro texture has a much higher association than micro texture, none the less micro texture of Mentor has also been implicated and more and more cases are likely to be discovered.</td>
<td>1) Please note polyurethane is not a textured surface: its tri-dimensional matrix is not equivalent, nor comparable to a bidimensional silicone surface. As such, it interacts very differently with the surrounding tissues at a mechanical and biological level.
2) All texture classification methods are arbitrary. Several different classification proposals have been published in the recent scientific literature or considered by national authorities; however, the only official shared texture classification worldwide is the ISO 14607:2018.
3) the cause of BIA-ALCL is still unknown. As mentioned, several hypotheses are being researched, but none has yet been proven, and scientists are looking at BIA-ALCL as a multi-factorial disease now.
Lastly, it is true that an increasing number of cases with Mentor implants have been reported. On the occasion of the 1st Consensus world conference on BIA ALCL, a nearly 100% increase of cases of BIA-ALCL with Mentor implants in Australia was disclosed (from 7 in 2018 to 13 in 2019).
In general, awareness leads to increased diagnoses, and this goes to show that black-and-white claims that certain implants have absolutely no possibility of being associated with BIA-ALCL, cannot be trusted.</td>
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<td>In America and Canada, they use about 80% Smooth and only 20% Textured and in both studies all their cases (1:27,000) were in Textured and not a single case in Smooth. Now there has got to more than simply 'bad luck' at play here.</td>
<td>The remarkably higher incidence of BIA-ALCL with textured implants has never been denied, considering roundabout 84% of cases of BIA-ALCL worldwide are with Allergan Biocell textured implants. However, the statistical evidence linking implants and ALCL cannot be assumed scientifically as proof of causation in relation to any surface type.
From a different, equally relevant point of view, according to decades of peer-review literature, the rates of occurrence of capsular contracture, as well as of other complications such as rotation and dislocation, vary in relation to the implant surface:[9]
<table>
<tr><td></td><td>Smooth implants</td><td>Textured implants</td><td>PU-covered implants</td></tr>
<tr><td>Capsular contracture rate</td><td>30-50%</td><td>15-30%</td><td>0-9%</td></tr>
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In most of the large studies, the capsular contracture rate for polyurethane-foam-covered implants is as low as 0-3 %.
Recent studies have shown that POLYTECH Microthane® implants are a safe choice for both primary breast augmentation and 2-stage breast reconstruction, and have lower complications even in case of radiation treatment, which is known to dramatically increase the risk of capsular contracture.[10] These studies also show a very low rate of seroma, thanks to mechanism of action of the polyurethane foam.
So even if smooth implants could in theory reduce the small risk of BIA-ALCL - but this has not yet been proven - they have a very high risk of other complications and thus of early reoperation.</td>
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[9] Vazquez and Pellon, (2007); Handel, *et al.* (2006); Handel (2006); Handel *et al.* (1991) Kjoller *er al.* (2002); Malata *et al.* (1997) Tebbetts (2001) Szycher and Siciliano (1991).

[10] Pompei *et al.*, (2017); Pompei (2016).

Early diagnosis and prompt removal of Implants and Capsule may be enough to cure patients but some may need more aggressive treatment and comprehensive including PET scans to identify the spread of the disease.	When diagnosed early, BIA-ALCL is commonly indolent and slow growing with an excellent prognosis, particularly when treated with surgery. According to Magnusson *et al.* (2019) and Clemens *et al.*, (2019), less than 5% need a more aggressive treatment.[11]
The recommendation for patients who already have Textured Implants is it not to remove them but monitor the patients carefully by annual examination and MRI as part of annual investigation.	No authority has ever recommended the prophylactic removal of any implant type. As stated above, women should attend regular checkups with their doctors – at least once a year. Patients who experience problems, aesthetic impairment or pain following breast implant surgery, should immediately inform their surgeon, and consider the available solutions. For more information on BIA-ALCL screening after breast surgery with implants, consult the *NCCN Consensus Guidelines 2019*. The 2019 update to the NCCN BIA-ALCL guidelines represents the most evidence-based approach to the disease based on the most current research. NCCN guidelines remain the recognized standard for diagnosis and treatment and ensure that patients are managed in a timely and appropriate fashion.

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[11] Magnusson *et al.* (2019); Clemens *et al.* (2019).