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Update on RIVM-report 2015-0100 'Silicone breast implants in the Netherlands - A market surveillance study'

State of affairs February 2018

On June 9th, 2016 RIVM published the results of a study on breast implants (RIVM report 2015-0100), commissioned by the Dutch Health and Youth Care Inspectorate. RIVM performed laboratory analyses on the implants and evaluated the technical files of ten manufacturers. The Inspectorate urgently called upon the manufacturers to clarify some of the laboratory findings and to resolve shortcomings in the technical files. In October 2017, a first update was published on the laboratory testing. This update also included a table with the names and corresponding identification numbers of the manufacturers, as the manufacturers had agreed to lift their anonymity in order to obtain transparency.
This document is the second update and provides an update on the assessment of the technical files.

Assessment of updated technical files

Since June 2016, breast implant manufacturers have been working on improving their technical files in consultation with their notified bodies. The Inspectorate commissioned RIVM to carry out a follow-up study on the updates made in the technical files. Manufacturers were requested to submit the updated documentation for the file items that did not score 'good' during the initial assessment reported in RIVM report 2015-0100. File items that were scored as 'good' in the initial report were excluded from the re-assessment. In total, 63 file items were requested from nine manufacturers. Manufacturer SBI05 (Perouse Plastie SAS) was excluded from the re-assessment. Following an acquisition of the company by Mentor Medical Systems BV, a commercial business decision was made to discontinue the PERTHESE® breast implants and Perouse Plastie SAS stopped placing products on the EU market in 2013. Consequently, the documentation had not been updated after publication of the RIVM report.

Methodology

The assessment of the file items was performed using the method as described in RIVM report 2015-0100. In short, a form was developed in order to enable a structured and uniform assessment of the files. The form included file items (e.g. risk analysis), which were in turn subdivided into sub-items (e.g. risk control/mitigation). For every sub-item, presence of adequate information was scored with yes/no/partial, or similar scoring options as relevant to the particular sub-item. The overall score for file items was obtained as the sum of the sub-item scores. The sum translated into a 'good', 'moderate' or 'insufficient' score. The re-assessment was performed using the same assessment form as for the initial assessment and by two assessors independently. The two assessments were compared during a meeting between the two assessors. During that meeting, all discrepancies were discussed and a decision was made on the final score.

The manufacturers were given the opportunity to check the assessment results for factual inconsistencies. During this check, the manufacturer could refer to information in the submitted documentation that, in their view, adequately addressed an aspect that did not score as 'good' according to the assessment by RIVM.
Furthermore, the manufacturers were given the opportunity to submit additional documentation to address a shortcoming, provided that this documentation already existed in April 2017 when it was requested for this follow-up study and was erroneously not included at the time.
The responses from the manufacturers, including additionally submitted information, were analysed. Where they solved shortcomings, the assessments were updated.
Subsequently, the assessment results were sent to the notified bodies of the manufacturers. They were given the opportunity to comment on items that RIVM did not score as 'good'. The responses from the notified bodies were assessed in conjunction with the data submitted by the manufacturers. Where appropriate, the assessment score was adjusted.
The final assessment score was sent to the manufacturers and the notified bodies in December 2017, together with an explanation regarding the score, with the request to resolve any remaining shortcomings.

Results
The results of the current assessment are presented in Table 1. To facilitate comparison with the previous assessment, the results of both the initial and the current assessment are included in Table 2.

In general, the revised technical documentation submitted by manufacturers showed improvement in the scores for 50 of the 63 file items that did not score 'good' in the initial assessment. In 12 cases, the score ('insufficient' or 'moderate') remained the same. In one case, the assessment score for the file item 'risk analysis' was lower than in the initial assessment. Although often a number of sub-items were improved, the improved overall score for the file item did not always translate to a change in the outcome 'insufficient' or 'moderate'.
All updated files were now scored as 'good' for the general description of the implant. The files of three manufacturers still included one or two file items that were scored as 'insufficient'. All files scored 'moderate' for one up to five file items. None of the files scored 'good' on all file items.
An example of a remaining shortcoming in some cases was the absence of the symbol "caution" on the label, indicating that the IFU should be consulted for cautionary information such as warnings and precautions. This symbol has a different meaning than the symbol "consult the instructions for use" that was usually present, which is only a general reference to the IFU.
Other examples of remaining shortcomings are limited information on the tests performed (test protocols) for biocompatibility and mechanical testing. For the clinical evaluation, the substantiation of the equivalence with other implants, was not always adequately addressed.

A response was received from seven manufacturers for the check on factual inconsistencies. Examples of additional information submitted by the manufacturers that led to an improved score are test protocols and test results. Several manufacturers provided additional information which

was from a later date than the submission in April 2017. Therefore, this information was not included in the re-assessment. However, it did indicate that the manufacturers were still further addressing shortcomings and improving their technical documentation.

The feedback from notified bodies led to an improvement in the score once, in relation to information on test protocols.
The notified bodies were explicitly asked to provide feedback on two sub-items where shortcomings had remained in a relatively large number of cases, i.e. the requirement to have "criteria for the necessity to take action" in the PMS procedure and the level of detail required for safety and performance claims in the Clinical Evaluation Report. In both instances, the notified bodies indicated that they agreed with the assessment criteria used by RIVM. The requirement for criteria to take action in the PMS procedures is now explicitly included in the text of the new medical device regulations. Notified bodies indicated they are intending to implement this requirement in their assessment of PMS procedures in the transition process to the new regulations.

Conclusions
The reassessment of the updated technical files for SBIs showed a considerable improvement in the quality of the documentation. Nevertheless, further improvement of the quality of the technical documentation can be achieved, since none of the files were scored as 'good' on all items.

Transparency of study results
The results in the 2016 RIVM report are anonymized. In order to obtain transparency, the Inspectorate called upon involved manufacturers to agree with lifting the anonymity. Following discussion with each manufacturer, agreement was reached on publishing the numbers and corresponding manufacturer names, see Table 3.

Table 1: Overview of the re-assessment of silicone breast implant files (2017)

File item	SBI01	SBI02	SBI03	SBI04	SBI06	SBI07	SBI08	SBI09	SBI10
Device description	-	-	-	-	G	G	G	G	-
IFU and label	M	M	M	M	M	M	G	G	M
Risk analysis	I	G	-	G	G	I	G	M	G
Biocompatibility	M	-	G	M	M	I	-	G	G
Mechanical testing	G	G	G	G	M	G	G	G	G
Clinical evaluation	M	I	M	M	G	G	M	G	G
PMS procedure	M	M	M	M	M	M	G	M	-
S&A PMS data	-	G	-	M	G	-	G	-	-
Vigilance procedure	G	M	-	G	M	-	G	-	-

Abbreviations: PMS – post-market surveillance; S&A – summary and analysis; SBI – silicone breast implant.
G = Good; M = Moderate; I = Insufficient; - = No reassessment (initially Good)

Table 2: Overview of the re-assessment of silicone breast implant files (2017), compared with the initial assessment (2016)

File item	SBI01		SBI02		SBI03		SBI04		SBI06		SBI07		SBI08		SBI09		SBI10	
	2016	2017	2016	2017	2016	2017	2016	2017	2016	2017	2016	2017	2016	2017	2016	2017	2016	2017
Device description	G	-	G	-	G	-	G	-	M	***G***	M	***G***	M	***G***	I	***G***	G	-
IFU and label	I	***M***	I	***M***	I	***M***	M	M	M	M	I	***M***	I	***G***	M	***G***	I	***M***
Risk analysis	I	I	I	***G***	G	-	M	***G***	M	***G***	M	I	I	***G***	I	***M***	M	***G***
Biocompatibility	I	***M***	G	-	I	***G***	I	***M***	I	***M***	I	I	G	-	M	***G***	I	***G***
Mechanical testing	M	***G***	I	***G***	I	***G***	I	***G***	M	M	M	***G***	M	***G***	I	***G***	M	***G***
Clinical evaluation	M	M	I	I	I	***M***	M	M	I	***G***	I	***G***	M	M	M	***G***	M	***G***
PMS procedure	I	***M***	I	***M***	M	M	I	***M***	I	***M***	I	***M***	I	***G***	M	M	G	-
S&A PMS data	G	-	I	***G***	G	-	I	***M***	I	***G***	G	-	I	***G***	G	-	G	-
Vigilance procedure	M	***G***	M	M	G	-	M	***G***	I	***M***	G	-	I	***G***	G	-	G	-

Abbreviations: IFU - instructions for use; PMS – post-market surveillance; S&A – summary and analysis; SBI – silicone breast implant.
G = Good; M = Moderate; I = Insufficient; - = No reassessment (initially Good). Improvement of the assessment score is indicated in bold and italic.

Table 3: File numbers and corresponding names of the manufacturers

Number	Manufacturer
SBI01	Groupe Sebbin SAS, France
SBI02	Nagor Ltd, UK
SBI03	Polytech Health & Aesthetics GmbH, Germany
SBI04	Allergan, UK
SBI05	Pérouse Plastie SAS, France
SBI06	Establishment Labs SA, Costa Rica
SBI07	Laboratoires Arion SAS, France
SBI08	Silimed, Brazil
SBI09	Eurosilicone SAS, France
SBI10	Mentor Medical Systems BV, Netherlands