Agence nationale de sécurité du médicament et des produits de santé

Meeting minutes

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Division: Division for therapeutic medical devices and cosmetics
Unit: Consumer medical devices and cosmetics
Head of department: Brigitte Heuls

TEMPORARY SPECIALIST SCIENTIFIC COMMITTEE

"Breast implant biocompatibility evaluation strategy"

Meeting of 15/03/2016

Participants	Status	Present	Absent /excused
Brigitte Heuls	Director of the division for therapeutic medical devices and cosmetics (DMTCOS)	☒	
Thierry Thomas	Deputy Director-DMTCOS	☒	
Hélène Duvignac	Consumer medical devices and cosmetics team manager	☒	
Cécile Verdier	Expert toxicologist-DMTCOS	☒	
Joëlle Amédée	Member	☒	
Pierre Cuq (video)	Member	☒	
Fabrice Ganachaud (telephone)	Member	☒	
Daniel Perdiz	Member	☒	
Muriel Vayssade	Member	☒	
Xavier Garric (video)	Occasional expert	☒	

Updates	Subjects discussed	Action	EU opinion required prior to publication YES/NO	PDI YES/NO
1.	**Introduction** **Agenda approval**	Adoption	N	N
2.	**Summary of manufacturer biocompatibility data** **First meeting summary (separate arguments)** **Combination of arguments**	Adoption	N	N
3.	**Discussion on our direction for interpreting manufacturers' arguments**	Discussion	N	N
4.	**Conclusions – Round table**	Adoption	N	N

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Meeting procedure

Note : The official version is the french version. Translation into English language is for information only.

1. **Introduction and agenda approval**

The agenda is approved by the experts.

2. **Summary of manufacturer biocompatibility data**

First meeting summary: Adoption of the experts' opinions on the relevance of the individual arguments

The work during the meeting of 01/02/16, during which the TSSC experts voted on the arguments for not carrying out biocompatibility tests, is summarised.

Combination of arguments

The objective of the TSSC meeting of 15/03/16 is to carry on with the work on the combinations of arguments provided by manufacturers to justify not carrying out biocompatibility tests.

WORKING METHODOLOGY PROPOSAL		DELIVERABLES
Step 1	Main arguments versus biological effects or opposite	**DELIVERABLE 1:** TSSC's opinion of 01/02/16 on the admissibility of each argument (vote)
Step 2	Combination of arguments per biological effect	**DELIVERABLE 2:** **TSSC's opinion of 15/03/16** on the combination of arguments per biological effect (vote)
Step 3	Recommendation on the strategy to be implemented to demonstrate textured breast implant biocompatibility	**DELIVERABLE 3:** Official line **TSSC opinion of 15/03/16**

The results of the votes are given in the tables below. There are 5 expert's votes for each argument.

Biological effects	Number of combinations of arguments analysed	RESULT OF THE VOTES ON ALL COMBINATIONS OF ARGUMENTS BY BIOLOGICAL EFFECT N: no A: abstention Y: yes
Carcinogenicity	4	20N
Immunotoxicity	1	2A, 1N, 2 "Y but"
Reproductive/developmental toxicity	1	5N
Biodegradation	4	20N
Toxicokinetics	3	15N

Discussion:

It is necessary to emphasise to manufacturers that they carry out fine and precise characterisation of their device. We speak in terms of texturing, microtexturing : the micrometric range in which the implants are classified should be determined. There again the combinations of arguments are not considered to be satisfactory or substantiated by the experts present.

3. Discussion on the proposed guideline for the textured breast implant biocompatibility demonstration strategy

The guideline is presented to the experts.

Discussion:

The experts say:

- That the guideline is well-written and clear.

- From a biological standpoint, a smooth and textured breast implant surface does not interact with tissue in the same way and should be subject to different biocompatibility tests. As a result, the arguments put forward by the manufacturers not taking the textured structure into account, are generally not admissible.

One expert asks what the purpose of the guideline is for manufacturers. The guideline could be seen as inciting them to conduct biocompatibility tests whereas the regulatory framework does not oblige them to do so.

An ANSM representative answers that legislation offers industrialists the possibility to provide reasons for not carrying out tests. As part of market control, the ANSM notes that an increasing number of industrialists do not carry out tests and they are within their rights not to do so. However, they should provide relevant arguments which today is not the case.
By investigating into breast implant biocompatibility, the ANSM aimed to demonstrate if the evidence of biocompatibility provided by companies was sufficient. Where it is considered to be insufficient, the ANSM will ask manufacturers to take actions in order to be in conformity.
The purpose of this guideline is to establish subjects for discussion, without making tests compulsory (which would constitute a breach of European rules).
In the case of breast implants, it should be kept in mind that it is not just because manufacturers carry out the tests recommended by the standard that the risk of ALCL is ruled out. Meeting the standard requirements is however a way for manufacturers to reduce risk as far as possible.
It is recalled that the ANSM invited manufacturers on 19 October 2015 to present the work of the ALCL TSSC, future work on biocompatibility and ongoing studies. The discussions were fruitful.

The experts say:

- That the guideline should not only focus on silicone implants. Polyurethane implants also belong to a large category: specify "raw material".
- What should be explained, where manufacturers decide to provide arguments for not carrying out tests, is that the arguments should be precise, detailed and thorough, and if this is not the case, the ANSM should strongly recommend that such tests be carried out.
- That the results of tests on smooth implants cannot be extrapolated to the case of textured breast implants. Smooth and textured implants do not interact with tissue in the same way and should undergo different types of tests.
- That the guideline should stipulate that texture breast implants must be shown to be biocompatible.
- That the argument put forward by some manufacturers as to bioequivalence with other breast implants of different brands is only acceptable if it is clearly demonstrated that the physical properties of the implant textures are identical; if this is not the case, the bioequivalence argument is not acceptable.
- Biocompatibility data on the whole implant or the shell is needed in order to include texturation.

An ANSM representative asks about manufacturers with a range of implants with different textures. Until now, it was accepted that if biocompatibility tests had been carried out on the "highest texturing", therefore as worst case, the results could be extrapolated to other less textured implants.
The experts say that an implant with different texturing is therefore an implant that should be subject to separate tests: the biological responses are not likely to be the same. Each texture requires separate tests.

4. Conclusions – Round table

The arguments provided by the manufacturers were therefore assessed separately or together by the TSSC experts in two meetings. Almost all of the arguments put forward by the manufacturers were considered to be unacceptable for justifying the lack of biocompatibility tests.
The ANSM must therefore come back to the manufacturers to inform them of that fact.
The guideline will be finalised once again and sent to the TSSC experts by e-mail.

No further meetings are scheduled for the breast implant biocompatibility evaluation strategy TSSC.