

DIRECTION DES DISPOSITIFS MEDICAUX
THERAPEUTIQUES ET DES COSMETIQUES

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Guideline for demonstrating textured breast implant biocompatibility

Notice to manufacturers

Regulatory and standards framework

Directive 93/42/EEC sets out the essential requirements, especially point 7.1, appendix I, for medical device compatibility with human tissue, which breast implants should meet in order to ensure a high level of health safety.

There are several standards in this field that manufacturers can refer to when claiming compliance with these essential requirements.

Standard ISO 10993-1 provides indications on the biological evaluation of medical devices according to the type and time of contact with surrounding tissue.

Standard ISO 14607, specific to breast implants, also recalls, in § 7.2.4, that the potential short- and long-term effects should be taken into account, and provides a list of tests to be used during preclinical evaluation by the manufacturer. The standard also states that the short- and long-term effects of the shell on surrounding tissue should be taken into account. Both standards are harmonised European standards which when applied confer presumption of compliance with the relevant regulatory essential requirements.

They both also state that justification for not carrying out tests can be provided or that it is not necessary to carry out tests given the past experience with the materials used.

Contents of the manufacturers' technical file for demonstration of biocompatibility

From establishment of these guidelines, it is expected that the following biological tests on the sterilised finished product be taken into account for breast implants or that the manufacturer provide scientific evidence for not conducting them:

- cytotoxicity,
- sensitization,
- irritation or intracutaneous reaction,
- (acute) systemic toxicity,
- subacute toxicity,
- genotoxicity,
- implantation.

It is also strongly advisable to carry out other tests as part of the risk assessment, such as:

- biodegradation,
- carcinogenicity,
- immunotoxicity,
- chronic toxicity,

- reproductive/developmental toxicity,
- toxicokinetics,
- or other organ-specific toxicity.

On the basis of these guidelines, it also results that textured implants should undergo separate tests from smooth implants, as the interaction of the textured shell of these implants with surrounding tissue is said to be different.

Considerations to be taken into account by breast implant manufacturers where biocompatibility tests recommended by harmonised European standards are not carried out.

Where tests recommended by harmonised standards ISO 10993-1 and ISO 14607 are not carried out, the manufacturer should provide reasons for this.

To this effect, the ANSM recommends that manufacturers having chosen to not carry out tests take the following into account during demonstration of biocompatibility:

- From a biological standpoint, a smooth surface and the different types of textured breast implant surface do not behave in the same way in contact with tissue. Each range of breast implant, according to shell texturing, should therefore be subjected to separate biocompatibility testing;
- Where biocompatibility tests are carried out, they should be carried out on sterilised breast implants (finished product) or on the sterile textured shell and on the breast implant gel.
- Physicochemical characterisation of the materials in the various parts of the breast implant, and extracts taken from a biocompatibility study, are an essential prerequisite to compiling a breast implant biocompatibility study plan;
- The texture of the breast implant shell is to be taken into account when demonstrating biocompatibility;
- Extrapolation of biocompatibility data for smooth breast implants is not sufficient for demonstrating the biocompatibility of textured breast implants;
- Using the same materials for smooth and textured implants is not a good enough reason for justifying the biocompatibility of the implants as the interaction between the bodily tissue and shell texture is not taken into account;
- Using raw materials equivalent to those used to make other breast implants is not sufficient to demonstrate the biocompatibility of a textured breast implant.
- Data from scientific literature available on silicone implant biocompatibility, where it is used to demonstrate the biocompatibility of a breast implant, should be completed with biocompatibility data on the finished breast implant, in order to take into account all potential changes to the raw materials during the manufacturing process;
- Use of clinical data on other implant brands is acceptable if the breast implants can be shown to be equivalent, including in terms of manufacture and the physicochemical characterisation of the shells;
- Clinical hindsight can be used to demonstrate the biocompatibility of breast implants if it provides information on biocompatibility, and if the clinical trials in question cover either the manufacturer's own products or products with which equivalence has been confirmed; the effect of changes made to the product, and the impact of changes in standards and regulations should be taken into account for the period in question.
- The results of clinical trials can be used if their aim is also to demonstrate breast implant biocompatibility. Otherwise, preclinical trials should also be provided;
- The appearance of new biological effects in humans from breast implants should be taken into account during post-marketing surveillance, and as a result should be included in the biocompatibility test results;

Conclusion

Consequently, the ANSM recommends that the items discussed in this document be taken into account by breast implant manufacturers in their biocompatibility tests.

The ANSM otherwise considers that unless acceptable arguments for not conducting the battery of tests put forward by the harmonised European standards are provided, they should be carried out both on the sterilised breast implants (finished product) or on the textured shell, and on the breast implant gel.