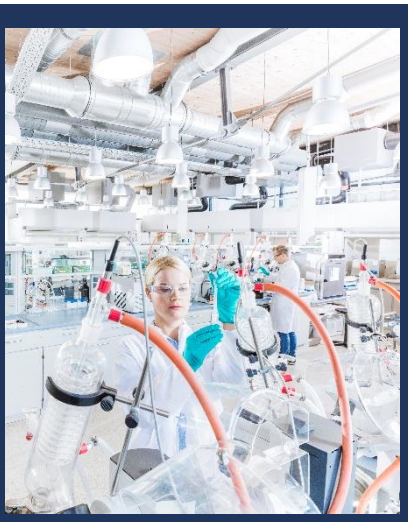
FACTSHEET

HOHENSTEIN

Chemical characterisation acc. to ISO 10993-18

The chemical characterisation of medical devices according to ISO 10993-18 is an essential part of the biological evaluation and risk assessment of medical devices. It serves as the basis for deciding whether and which further biocompatibility-related tests are necessary and thus forms an integral part of the overall biocompatibility tests as defined by the ISO 10993 series of standards.



Regulatory background

When a medical device is authorised, the general safety and performance requirements (GSPR) must be fulfilled. The fulfilment of these requirements is confirmed by a declaration of conformity. This is based on a prior conformity assessment, which is based on the technical documentation.The biocompatibility of the medical device must be verified as part of the technical documentation. Proof of biocompatibility is provided in accordance with the harmonised ISO 10993 series of standards for medical devices with direct and indirect contact to humans. Translated with DeepL.com (free version)

Relevance of ISO 10993-18 within the biocompatibility assessment

As part of the biocompatibility assessment of a medical device, the ISO 10993 series takes a risk-based approach. Chemical characterisation (ISO 10993-18) plays a key role here, as it analyses the chemical composition of the medical device and identifies potentially toxicologically relevant substances that could come into contact with the body. The aim of the investigation is to carry out a toxicological risk assessment (TRA) from the chemical data obtained. This is carried out in accordance with ISO 10993-17 and evaluates the risk of identified substances on the basis of known toxicological limit values. Thus, unnecessary in vivo tests (animal testing) can be avoided.

Technical requirements

In order to carry out a meaningful and reliable toxicological risk assessment, a high-quality and comprehensive chemical characterisation must first be carried out. To do this, it is necessary to cover the entire chemical spectrum. This is done by categorising substances into different substance classes:

Volatile organic compounds (VOC): boiling point < 250 °C

Substances with a low boiling point and high volatility. Due to these properties, mild analysis techniques such as gas chromatography (GC-MS) are suitable for the analysis.
Typical examples: Solvents such as toluene, ethanol, acetone, acetonitrile.

Semi-volatile organic compounds (SVOC): boiling point 250 - 400 °C

Substances with a more complex molecular structure, such as plasticisers or various additives. Due to the medium volatility, both gas chromatographic (GC-MS) and liquid chromatographic (LC-MS) analysis techniques are used here.
Typical examples: Phthalates, phenols, bisphenols, pesticides.

Non-volatile organic compounds (NVOC): boiling point > 400 °C

Substances with a large molecular mass and a complex structure. As a result, these substances often have a very high boiling point and cannot be separated using gas chromatography. Different liquid chromatographic analysis techniques (LC-MS) are used here.
Typical examples: Oligomers, additives with low volatility.

Inorganic substances (metals): are not classified by boiling point

Metals are analysed using inductively coupled plasma mass spectrometry (ICP-MS) after acid digestion or aqueous extraction.
Typical examples: all metallic materials and/or components

Conclusion

The chemical characterisation according to ISO 10993-18 is a central part of the biocompatibility assessment of medical devices and forms the basis for a toxicological risk assessment. It is used to identify potentially critical substances in order to avoid unnecessary animal testing. High-quality analysis requires the detection of the entire chemical spectrum, including volatile, semi-volatile, non-volatile and inorganic substances.

Description of the test

To determine extractable and leachable substances (Extractables & Leachables), a medical device is extracted in an aqueous solution, in semi-polar and/or non-polar solvents. The extraction conditions depend on the application, contact type and contact duration of the product.

The analytical evaluation threshold (AET) is calculated on a product-specific basis and defines the concentration above which a soluble substance must be identified and toxicologically evaluated.

This is followed by semi-quantitative screening using various analytical methods. The detected substances are identified by comparing them with calibrated data and databases. The semi-quantitative determination is carried out using reference substances (surrogates).

The determination of extractable elemental substances is conducted on aqueous extracts via ICP-MS using appropriate element standards.

The test report contains

- Calculation of the AET value (Analytical Evaluation Threshold) depending on the application of the product
- List of extractable chemical substances above the AET value incl. identification category and semi-quantitative concentration information

Requirements for the test sample

General

- Preferably send end products in their original packaging for testing
- Analysis is usually carried out on the entire product; components can be analysed separately or individually on request
- When sending several samples, ensure that ingredients are not transferred to other samples (pack separately)
- Provide sufficiently precise description (name, material composition, article number, UDI, etc.) of the test sample

Quantity of material

- In general 1 product per extraction agent and analysis technique

Test duration

- Usually approx. 20-30 working days (depending on the analysis technique ordered); confirmation of date after receipt of test sample