FAQ Pre-clinical characterization of Hydroxyapatite powders

according to ISO 13779-6

by Nicola Döbelin, PhD
Team Leader Bioceramics
nicola.doebelin@rms-foundation.ch

The European **Medical Device Regulation (MDR)** lays down regulatory rules for market access of medical devices for human use. In Annex II section 6.1, the framework requires physical and chemical characterizations of the device as well as proof of conformity with product specifications.

Deviations from conformity with product specifications can be detected at an early stage if the raw materials are already checked for purity and composition. In addition, tests on raw materials document consistent material properties, which is a prerequisite for a functioning manufacturing process.

Specifications for physical and chemical properties of **Hydroxyapatite (HAp) powders** used as a raw material for the manufacturing or coating of surgical implants can be found in **ISO 13779-6**. This standard lists a series of analyses and specifies limits for the tested properties that a product must meet for conformity with the standard.

Q *Which pre-clinical physical / chemical characterizations must be performed?*

A ISO 13779-6 requires the following analyses:

- Calcium to phosphorus molar ratio (Ca/P)
- Trace elements, including trace elements in excess of 500 mg/kg with their mass fractions
- Qualitative and quantitative determination of foreign phases
- Crystallinity ratio
- Ground or atomized state of the powder (powder morphology)
- Granulometry
- Calcination loss at 1000°C

Q *Can RMS Foundation perform these characterizations?*

A **Yes**, we offer all these analyses as an attractive package, including a report with detailed descriptions of the test procedures, as well as statistical evaluation and critical assessment of the results. All test methods are validated and accredited according to **ISO/IEC 17025:2017**.

Q *What kind of samples should be used for the characterization?*

A The samples must represent the raw material in the form in which it is used for the production of medical devices. Take samples from the top, middle, and bottom of the container. Pack the specimens securely protected from moisture, light, and mechanical damage.

Q How many samples should be tested?

A The results of the analyses must be **statistically robust**. This means that reliable mean values and standard deviations across several batches must be determined. Therefore, **multiple measurements are indispensable**. We recommend one of the following sampling plans:

Sampling plan	Batches	Samples per batch	Samples total
Gold	3	3	9
Economic	3	2	6
Minimum	3	1	3

The «**Gold**» plan allows to determine a robust mean value and standard deviation of the results. Outliers can be identified reliably.

The «**Economic**» plan fulfills minimum requirements to determine the mean value and standard deviation according to statistical best practice.

The «**Minimum**» plan allows to determine a mean value and standard deviation of the results, but the reliability of the statistics is low. A risk assessment based on this standard deviation is not recommended.

Q How much material is required for the analyses?

A These are the material requirements for each analysis and sampling plan:

Analysis	Method	Gold	Economic	Minimum
Ca/P molar ratio	XRD	9 x 1.0 g	6 x 1.0 g	3 x 1.0 g
Trace elements	ICP-MS	9 x 0.2 g	6 x 0.2 g	3 x 0.2 g
Foreign phases	XRD	9 x 1.0 g	6 x 1.0 g	3 x 1.0 g
Crystallinity ratio	XRD	9 x 1.0 g	6 x 1.0 g	3 x 1.0 g
Powder morphology	Electron microscopy	9 x 0.1 g	6 x 0.1 g	3 x 0.1 g
Granulometry	Laser diffraction or sieving	9 x 5.0 g	6 x 5.0 g	3 x 5.0 g
Calcination loss	Thermogravimetry	9 x 10.0 g	6 x 10.0 g	3 x 10.0 g

Q How much do the analyses cost?

A The costs vary depending on the nature of the product and the selected sampling plan. Please contact us by e-mail or phone to **request a quote**. You can help us by providing the following information in your inquiry:

- The type of product (form, composition)
- The sampling plan you wish to receive a quote for (we can provide multiple quotes)
- The region you plan to register your product (EU/CH, USA, other) or whether the characterizations will be used for development purposes

Our experts can also advise you on the planning of the characterizations in a consulting project. Please contact us to request a non-binding quote.