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# Dentistry — Implantable materials for bone filling and augmentation in oral and maxillofacial surgery — Contents of a technical file

*Art dentaire — Matériaux implantables pour le remplissage et l'augmentation osseuse en chirurgie orale et maxillofaciale — Contenu d'un dossier technique*

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# Foreword

ISO (the International Organization for Standardization) is a worldwide federation of national standards bodies (ISO member bodies). The work of preparing International Standards is normally carried out through ISO technical committees. Each member body interested in a subject for which a technical committee has been established has the right to be represented on that committee. International organizations, governmental and non-governmental, in liaison with ISO, also take part in the work. ISO collaborates closely with the International Electrotechnical Commission (IEC) on all matters of electrotechnical standardization.

International Standards are drafted in accordance with the rules given in the ISO/IEC Directives, Part 2.

The main task of technical committees is to prepare International Standards. Draft International Standards adopted by the technical committees are circulated to the member bodies for voting. Publication as an International Standard requires approval by at least 75 % of the member bodies casting a vote.

Attention is drawn to the possibility that some of the elements of this document may be the subject of patent rights. ISO shall not be held responsible for identifying any or all such patent rights.

ISO 22794 was prepared by Technical Committee ISO/TC 106, *Dentistry*, Subcommittee SC 8, *Dental implants*.

# Introduction

Different materials used for the preservation of masticatory function, such as dental restorative materials and dental implants are subject to standards and regulations, either in existence or in preparation, designed to evaluate the performance of these products.

Implantable materials for bone filling and augmentation in oral and maxillofacial surgery are not covered by the procedures for evaluating and testing dental restorative materials and dental implants; it is necessary to develop a new standard for these materials.

The aim of this International Standard is to define the content of a technical file that demonstrates safety and effectiveness of bone filling and augmentation materials used in oral and maxillofacial surgery.

# Dentistry — Implantable materials for bone filling and augmentation in oral and maxillofacial surgery — Contents of a technical file

## 1 Scope

This International Standard applies to implantable materials, whether resorbable or non-resorbable, used as dental devices for filling and augmenting bones in oral and maxillofacial surgery. Products that are essentially pure (> 90 %) hydroxyapatite are not covered by this International Standard.

Evaluation includes the physico-chemical, mechanical, biological and clinical aspects and behaviour of these implantable dental materials.

Materials such as autografts, allografts and membranes, and products for which the primary intended use is to deliver a medicinal product, are not covered by this International Standard.

## 2 Normative references

The following referenced documents are indispensable for the application of this document. For dated references, only the edition cited applies. For undated references, the latest edition of the referenced document (including any amendments) applies.

ISO 1942:—[1], *Dentistry — Vocabulary*

ISO 10993-1:—[2], *Biological evaluation of medical devices — Part 1: Evaluation and testing within a risk management system*

ISO 10993-17, *Biological evaluation of medical devices — Part 17: Establishment of allowable limits for leachable substances*

ISO 11134[3], *Sterilization of health care products — Requirements for validation and routine control — Industrial moist heat sterilization*

ISO 11135:1994, *Medical devices — Validation and routine control of ethylene oxide sterilization*

ISO 11137:1995, *Sterilization of health care products — Requirements for validation and routine control — Radiation sterilization*

ISO 11607:2003, *Packaging for terminally sterilized medical devices*

ISO 13408-1, *Aseptic processing of health care products — Part 1: General requirements*

1) To be published. (Revises and replaces ISO 1942 parts 1 to 5:1989)

2) To be published. (Revision of ISO 10993:2003)

3) International Standard withdrawn.

ISO 14155:1996, *Clinical investigation of medical devices*

ISO 14937, *Sterilization of health care products — General requirements for characterization of a sterilizing agent and the development, validation and routine control of a sterilization process for medical devices*

ISO 14971, *Medical devices — Application of risk management to medical devices*

ISO 15223:2000, *Medical devices — Symbols to be used with medical device labels, labelling and information to be supplied*

EN 1041, *Information supplied by the manufacturer with medical devices*

## 3 Terms and definitions

For the purposes of this document, the terms and definitions given in ISO 1942 and the following apply.

**3.1**
**biocompatibility**

a) capability of a material to fulfil its function with an appropriate response for a specific application from the receiving host;

b) quality of being accepted in a specific living environment without adverse or unwanted side effects

**3.2**
**biomaterial**

a) material intended to interface with the biological system to evaluate, treat, augment or replace tissue, organ or function of the organism;

b) material specially prepared and/or presented to exhibit bioacceptability, biocompatibility or positive biocompatiblity

NOTE The implantable materials referred to in this document are all biomaterials.

**3.3**
**filling**
surgical placement of a biomaterial, resorbable or non-resorbable, into an intrabony cavity during oral and maxillofacial surgery

NOTE Intrabony cavity includes extraction socket.

**3.4**
**augmentation**
surgical placement of a biomaterial, resorbable or non-resorbable, to increase the volume of bone, usually on the sinus floor or the alveolar ridges

**3.5**
**resorption**
progressive elimination by cellular activity and/or dissolution of a material in a biological environment

**3.6**
**medicinal product**
substance that produces its intended effect by pharmaceutical means

## 4 Implantable materials

The development of implantable materials shall be considered with regard to the properties required for the intended purpose, taking into account the effects of manufacture, handling, sterilization and storage. Possible

reactions (intended or not) of implantable materials with human tissues and body fluids, other materials, other implants, substances, gases, radiation and electromagnetic fields shall be considered.

Implantable materials for bone reconstruction in oral and maxillofacial surgery are used either for filling or augmentation.

# 5 Technical file

## 5.1 Contents

The contents of a technical file shall include at least the following:

— details of the chemical composition and physical properties of the implantable material;

— its intended performance;

— its preclinical and clinical evaluation;

— details of its manufacture, sterilization and packaging;

— all information necessary for the user (as detailed later).

New materials, for which the following characterization methods may not be adequate, shall be characterized using techniques appropriate to the materials and the choice of technique shall be justified.

## 5.2 Chemical composition

As appropriate, the following shall apply.

The complete chemical composition, summing to 100 % by mass, including all additives, shall be described.

The crystalline and non-crystalline phases, phase purity, and the mass fractions of phases, using X-ray diffraction (XRD), Fourier transform infrared spectroscopy (FTIR) and/or differential scanning calorimetry (DSC), as appropriate, shall be described.

The composition description shall also include elemental analysis, identifying the cation to anion ratio (e.g., Ca/P, Ca/S) and/or the carbon/oxygen/nitrogen ratios (e.g., C/O/N), as appropriate, and all trace impurities relevant to the application.

Diffraction patterns, along with superimposed patterns of each phase as given for the relevant calcium salt and available from the International Center for Diffraction Data/Joint Committee on Powder Diffraction Standards (ICDD/JCPDS), shall be described.

NOTE Several standards that address the specifics of different materials are available and can be useful references for other bone-filling materials. See references [15], [16], [17], [18], [19].

## 5.3 Physical properties

The physical form of the material (e.g., granules, preformed porous or non-porous block or putty/paste intended to set *ex-vivo* or *in-vivo*) shall be described.

Dimensional specifications for the material shall be given.

The mass and volume of the material shall be described.

The material porosity (e.g., total porous volume and mean pore diameter) shall be given. A magnified photograph such as an SEM micrograph shall be included in the description.

Particle shape and size shall be described for materials that are used only as particulates (granules).

## 5.4 Intended applications, precautions, warnings and instructions

The intended applications for the material shall be described.

Precautions for use of the material shall be described. Examples include:

— not for load-bearing sites;

— effect on pediatric patients is not known;

— do not overfill site;

— do not disturb the material until it has hardened (for putty/paste materials).

Warnings for use of the material shall be described. Examples include:

— do not use the material in infected sites;

— do not use on patients with known allergies to components;

— do not implant a resorbable calcium salt material in a patient with a pre-existing calcium metabolism disorder (e.g., hypercalcemia);

— single-use only, do not resterilize or re-use;

— do not use if package is opened or damaged or if the expiry date has been exceeded;

— the material must be secured to prevent motion and migration; use in areas where the material can be adequately contained;

— use of a bone filling and augmentation material at the time of dental implant placement will require additional healing time before loading.

Instructions for use shall be described, including, at least, the following:

— instructions for site preparation;

— instructions for material preparation prior to implantation;

— procedure for proper placement and containment of the material;

— method of site closure;

— programme for patient follow-up care;

— guidance for the anticipated process of tissue healing and material resorption over time;

— advice on any possible risks to personnel handling the material and the appropriate precautions to be taken.

## 5.5 Preclinical and clinical evaluation

### 5.5.1 General

The details of an appropriate risk analysis, conducted according to the requirements in ISO 14971, shall be included. Evidence for the safety of the material shall be provided and, when necessary, all details of any preclinical and/or clinical tests and trials performed, according to the guidance in ISO 10993-1. Implantable

materials shall be evaluated to demonstrate that the intended performance is achieved. The extent to which the intended performance has been achieved shall be documented.

When a medicinal product is an integral part of an implantable material, the medicinal product shall be assessed according to pharmaceutical principles. Neither the intended function of the implantable material nor that of the medicinal product shall be affected by a combination of the two.

### 5.5.2 Preclinical evaluation

When appropriate, tests describing the following properties shall be reported:

— strength;

— elastic modulus;

— shear modulus;

— pH;

— dissolution/solubility;

— molecular weight distribution;

— viscosity.

Final sterilized materials in a simulated physiological environment shall be used for bench testing.

If the material is intended to set *in-vivo* then the details and results of the tests used for the evaluation of the following additional properties shall be included:

— working time;

— setting time;

— dimensional stability;

— setting reaction temperature;

— chemical analysis of the final material.

Biocompatibility:

Details of all aspects of the preclinical biological evaluation shall be included. Implantable materials shall undergo preclinical biological evaluation in accordance with the requirements of ISO 10993-1 by:

a) a compilation and critical analysis of relevant scientific literature and/or

b) analysis of data obtained from testing.

Preclinical testing of implantable materials shall simulate conditions of intended use whenever possible.

Animal testing:

New devices that have different critical specifications (e.g., chemistry, crystallininity, physical form, porosity, dissolution/solubility) should be tested in an animal model. Animal testing is usually necessary with novel materials and with established materials manufactured in a new way such that their specification is different from that of previously available products. Animal testing may also be necessary if new claims, specific to the performance of the material, are made.

### 5.5.3 Clinical evaluation

Details of all aspects of the clinical evaluation shall be included. Implantable materials shall undergo clinical evaluation by:

a) a compilation and critical analysis of relevant scientific and clinical literature covering the intended use of the materials and/or

b) analysis of data obtained from clinical investigation.

New materials that cannot be fully assessed by an animal study shall be further evaluated in a human clinical trial. Clinical trials are usually necessary with novel types of biologically active materials. Clinical trials shall be carried out in accordance with ISO 14155. Any claims regarding the clinical performance of the material shall be substantiated by the data obtained from the clinical trial.

## 5.6 Manufacture

Manufacturing processes shall be consistent with applicable regulations and/or International Standards. If required for regulatory purposes, manufacturing processes shall be described and evidence of their validation shall be provided.

Implantable materials shall be manufactured in such a way that the intended performance is achieved.

## 5.7 Materials of animal origin

In materials of animal origin, details of all measures taken to evaluate the risk of viral and/or transmissible spongiform encephalopathy (TSE) agent contamination and the tests undertaken to assess this risk, shall be included. The manufacturing process shall ensure that the risk of contamination by viruses and other transmissible agents be eliminated or reduced to an “acceptable” level. The animal source (species and herd) and the country of origin shall be identified.

NOTE Guidance to risk assessment and elimination can be found in references [20], [21], [22], [23], [24], [25].

## 5.8 Sterilization

### 5.8.1 Products supplied sterile

The sterility assurance level of terminally sterilized implantable materials shall be $10^{-6}$ or better. Sterilization processes shall be validated and routinely controlled. All details of the sterilization processes employed and their validation shall be included.

If implantable materials are to be sterilized by ethylene oxide, ISO 11135 shall apply, by irradiation, ISO 11137 shall apply, by steam, ISO 11134 shall apply, and by any other method validation shall be carried out according to ISO 14937.

If the manufacturer states that re-sterilization is acceptable, at least one validated method shall be specified.

### 5.8.2 Products supplied non-sterile

For implantable materials which are supplied non-sterile, the manufacturer shall specify at least one validated method of sterilization such that their functional safety is not adversely affected. If multiple sterilizations are not allowed, this shall be stated in the information provided by the manufacturer (see 5.10.1).

If the product has been aseptically processed, ISO 13408-1 shall apply.

### 5.8.3 Sterilization residuals

Testing for residuals of sterilization shall be in accordance with the principles set out in ISO 10993-17.

## 5.9 Packaging

### 5.9.1 Protection from damage in storage and transport

Details of packaging methods and materials shall be given and a sample package shall be provided.

Packaging shall be designed as specified by the manufacturer, so that under conditions for storage, transport and handling (including control of temperature, humidity and ambient pressure, if applicable), the packaging protects against damage and deterioration and the material is not adversely affected.

### 5.9.2 Maintenance of sterility in transit

Evidence of the maintenance of sterility of the material during transit shall be included. Implantable materials supplied in sterile conditions shall be packaged so that they remain sterile under normal storage, transport and handling conditions unless the package is damaged or opened.

For terminally sterilized products, packaging shall conform to ISO 11607.

## 5.10 Additional information supplied by the manufacturer

### 5.10.1 General

Samples of additional information supplied by the manufacturer shall be included. Information supplied by the manufacturer shall be in accordance with EN 1041. If symbols are used, they shall be in accordance with ISO 15223.

If multiple sterilizations are not allowed, this shall be stated in the information provided by the manufacturer.

### 5.10.2 Restrictions on combinations

If the implantable material is intended to be used in combination with other devices, any restrictions in the use of the combination shall be stated on the label or in the instructions for use and/or the manual.

### 5.10.3 Identification of implantable materials

In order to provide traceability, the following information shall be included on the label:

— name of product;

— manufacturer’s name or trademark;

— address of the manufacturer;

— batch code (lot number) or serial number;

— sterile (plus method of sterilization) or non sterile;

— storage recommendation;

— expiry date, if needed.

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