BS ISO 13175-3:2012

BSI Standards Publication

Implants for surgery — Calcium phosphates

Part 3: Hydroxyapatite and beta-tricalcium phosphate bone substitutes

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National foreword

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A list of organizations represented on this committee can be obtained on request to its secretary.

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Implants for surgery — Calcium phosphates —

Part 3: Hydroxyapatite and beta-tricalcium phosphate bone substitutes

Implants chirurgicaux — Phosphates de calcium —

Partie 3: Substituts osseux à base d'hydroxyapatite et de phosphate tricalcique bêta

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Contents

Page

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 13175-3 was prepared by Technical Committee ISO/TC 150, *Implants for surgery*, Subcommittee SC 1, *Materials*.

ISO 13175 consists of the following parts, under the general title *Implants for surgery — Calcium phosphates*:

— *Part 3: Hydroxyapatite and beta-tricalcium phosphate bone substitutes*

Introduction

Hydroxyapatite and β-tricalcium phosphate synthetic bone substitutes are now considered as an adequate alternative to autografts and allografts. Indeed, the synthetic origin of these devices guarantees that no transmittable disease will contaminate the patient. Moreover, hydroxyapatite and β-tricalcium phosphate have been shown to be osteoconductive which means that they will promote bone healing at the surface of the material if implanted in a bone site (see References [6] and [7]). Biocompatibility of hydroxyapatite and β-tricalcium phosphate is demonstrated by extensive literature (see Reference [8]).

The devices referred to in this part of ISO 13175 are of three types: synthetic monophasic hydroxyapatite or β-tricalcium phosphate bone substitutes and biphasic hydroxyapatite/β-tricalcium phosphate bone substitutes. The hydroxyapatite/β-tricalcium phosphate ratio influence the dissolution rate of the material: the higher the β-tricalcium phosphate content, the higher the dissolution rate (see References [9] to [11]).

The healing process into the bone substitutes is not only related to the material osteoconductive potential, it is also related to the porosity structure (see References [12] to [16]). It is necessary that macroporosities are large enough and interconnected for bone ingrowth to take place into the whole volume of the implant. Porosities have also an influence on the resorption rate of the ceramic: the higher the number of microporosities, the higher the dissolution rate (see Reference [14]).

As bone substitutes are not intended for bearing heavy loads, their mechanical properties are not essential. However, most of the time blocks have to be reshaped by the surgeon to fit the shape of the bone cavity. The bone substitute shall have sufficient mechanical properties to be machined.

INTERNATIONAL STANDARD **ISO 13175-3:2012(E)**

Implants for surgery — Calcium phosphates —

Part 3: Hydroxyapatite and beta-tricalcium phosphate bone substitutes

1 Scope

This part of ISO 13175 specifies requirements for monophasic hydroxyapatite bone substitutes, monophasic β-tricalcium phosphate bone substitutes and biphasic hydroxyapatite/β-tricalcium phosphate bone substitutes in the form of blocks or granules.

This part of ISO 13175 is not applicable to cell-seeded bone void fillers, calcium phosphate cements or bone void fillers containing materials other than hydroxyapatite and β-tricalcium phosphate.

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 2591-1, *Test sieving — Part 1: Methods using test sieves of woven wire cloth and perforated metal plate*

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

ISO 13320, *Particle size analysis — Laser diffraction methods*[1)]

ISO 13383-1, *Fine ceramics (advanced ceramics, advanced technical ceramics) — Microstructural characterization — Part 1: Determination of grain size and size distribution*[2)]

ISO 13779-3, *Implants for surgery — Hydroxyapatite — Part 3: Chemical analysis and characterization of crystallinity and phase purity*

ISO 15901-1, *Pore size distribution and porosity of solid materials by mercury porosimetry and gas adsorption — Part 1: Mercury porosimetry*

ISO 80000-1, *Quantities and units — Part 1: General*

3 Terms, definitions and symbols

3.1 Terms and definitions

For the purposes of this document, the following terms and definitions apply.

1) Replaces ISO 13320-1.

2) To be published.

3.1.1
α tricalcium phosphate
α-TCP
chemical compound with a crystallographic structure characterized by ICDD PDF[3] 09-0348

NOTE 1 to entry: The chemical formula is $Ca_3(PO_4)_2$.

3.1.2
β tricalcium phosphate
β-TCP
chemical compound with a crystallographic structure characterized by ICDD PDF 09-0169

NOTE 1 to entry: The chemical formula is $Ca_3(PO_4)_2$.

3.1.3
bone substitute
device intended to fill bony voids or gaps caused by trauma or surgery

3.1.4
hydroxyapatite
HA
chemical compound with a crystallographic structure characterized by ICDD PDF 09-0432 or ICDD PDF 72-1243

NOTE 1 to entry: The chemical formula is $Ca_{10}(PO_4)_6(OH)_2$.

3.1.5
interconnected pore
pore which communicates with one or more other pores

3.1.6
macropore
pore with one of its dimensions larger than 10 μm

3.1.7
micropore
pore with no dimension larger than 10 μm

3.1.8
porosity
ratio of total pore volume to apparent volume of the block or granule

3.1.9
tetracalcium phosphate
TTCP
chemical compound with a crystallographic structure characterized by ICDD PDF 25-1137 or ICDD PDF 70-1379

NOTE 1 to entry: The chemical formula is $Ca_4(PO_4)_2O$.

3.1.10
osteoconductive material
material with the ability to serve as a scaffold on which bone cells can attach, migrate (meaning move or "crawl"), and grow and divide

NOTE 1 to entry: Osteoconductivity is a passive property.

3) International Centre for Diffraction Data Powder Diffraction File.

3.1.11
calcium oxide
CaO
chemical compound with a crystallographic structure characterized by ICDD PDF 4-0777 or ICDD PDF 82-1690

3.1.12
β-tricalcium phosphate density
$d_{\beta TCP}$
theoretical density of dense β-tricalcium phosphate, equal to 3,07 g cm^{-3}

3.1.13
hydroxyapatite density
d_{HA}
theoretical density of dense hydroxyapatite, equal to 3,15 g cm^{-3}

3.2 Symbols

d_r	bulk density of the synthetic bone substitute
d_{th}	theoretical density of the synthetic bone substitute
m	mass of the synthetic bone substitute
V	volume of the synthetic bone substitute

4 Requirements

4.1 Trace elements

The limits of specific trace elements for hydroxyapatite and β-tricalcium phosphate bone substitutes are given in Table 1.

Either inductively coupled plasma/atomic emission spectrometry (ICP/AES), inductively coupled plasma/mass spectroscopy (ICP/MS), atomic absorption spectroscopy (AAS), or the method specified in ISO 13779-3 shall be used to quantify trace elements. The method used shall be specified.

Table 1 — Limits of specific trace elements

Element	**Maximum limit** mg/kg
Arsenic	3
Cadmium	5
Mercury	5
Lead	30
Heavy metals	50

Method 1 of the United States Pharmacopeia “Heavy metals <231>” should be used to quantify heavy metals. It is also possible to use one of the methods described above for the quantification of trace elements to assess the heavy metal content by considering that the total amount of heavy metals is the sum of the following elements: lead, mercury, bismuth, arsenic, antimony, tin, cadmium, silver, copper and molybdenum. The method used shall be specified.

Any impurity with a ratio of more than 1 000 mg/kg shall be identified, quantified and its influence on bone healing shall be assessed. The influence of this impurity on biocompatibility shall be assessed according to ISO 10993-1.

Any additional additive shall be identified, quantified and its influence on bone healing and biocompatibility shall be justified or assessed in accordance with ISO 10993-1.

4.2 Qualitative and quantitative determination of crystalline phases

4.2.1 General

Composition and phase purity shall be controlled by the quantification of the phases by X-ray diffraction (XRD) in accordance with ISO 13779-3.

4.2.2 Hydroxyapatite monophasic bone substitutes

Hydroxyapatite mass fraction shall be not less than 95 % of the crystalline phases. The CaO mass fraction shall be not more than 1 % of the crystalline phases.

Hydroxyapatite mass fraction is calculated according to Formula (1):

$$MF_{HA} = 100\% - MF_{\beta TCP} - MF_{\alpha TCP} - MF_{TTCP} - MF_{CaO} \quad (1)$$

where

MF_{HA} is the mass fraction of crystalline HA;

$MF_{\beta TCP}$ is the mass fraction of crystalline β-TCP;

$MF_{\alpha TCP}$ is the mass fraction of crystalline α-TCP;

MF_{TTCP} is the mass fraction of crystalline TTCP;

MF_{CaO} is the mass fraction of crystalline CaO.

The mass fraction of any phase shall be considered as zero if its value is under the detection threshold.

4.2.3 Biphasic bone substitutes

The ratio between hydroxyapatite and β-tricalcium phosphate shall be specified with a tolerance of ± 5 % (absolute) of the mass fraction of crystalline phases.

EXAMPLE A composition of 60 % HA and 40 % TCP means that the composition can be (65 % HA and 35 % TCP) to (55 % HA and 45 % TCP).

Qualitative determination of the mass fraction of other crystalline phases: if α-tricalcium phosphate (α-TCP) can be detected, this information shall be indicated on the report.

4.2.4 β-tricalcium phosphate monophasic bone substitutes

The β-tricalcium phosphate mass fraction shall be not less than 95 % of the crystalline phases.

The β-tricalcium phosphate mass fraction shall be calculated according to Formula (2):

$$MF_{\beta TCP} = 100\% - MF_{HA} \quad (2)$$

The mass fraction of HA shall be considered as zero if its value is under the detection threshold.

Qualitative determination of other crystalline phases: if α-tricalcium phosphate (α-TCP) can be detected, this information shall be indicated on the report.

The presence of other phases shall be assessed by infrared spectroscopy (FTIR) in accordance with ISO 13779-3.

4.3 Form and shape

The physical form of the bone substitute (granules or pre-formed block) shall be specified.

Dimensional specifications shall be given for all device configurations as follows.

— Dimensions for the blocks.

— Dimensions of granulates: the laser diffraction method in accordance with ISO 13320 or sieving method in accordance with ISO 2591-1 shall be used to determine granule dimensions. Parameters D10, D50 and D90 (for laser diffraction) or minimum and maximum dimensions (for sieving) of the granules shall be specified.

The volume of the bone substitute shall be specified on the packaging.

4.4 Porosity

4.4.1 Total porosity ratio

The minimum and maximum porosity ratio of the bone substitute shall be specified. It shall be calculated according to Formula (3):

$$P = 100 - \left(\frac{d_r}{d_{th}} \cdot 100 \right) \tag{3}$$

where

P is the porosity ratio in %.

d_r shall be determined by measuring the dimensions and the mass of a parallelepiped bone substitute having a minimum volume of 2 cm^3. The mass shall be measured with a balance capable of weighing to an accuracy of 0,02 g and the dimensions shall be measured with a vernier calliper capable of measuring to an accuracy of at least 0,02 mm. The volume, V, of the bone substitute shall then be calculated with the measured dimensions and d_r shall then be calculated according to Formula (4):

$$d_r = \frac{m}{V} \tag{4}$$

d_{th} shall be calculated according to Formula (5):

$$d_{th} = \frac{\frac{MF_{HA}}{d_{HA}}}{\frac{MF_{HA}}{d_{HA}} + \frac{MF_{\beta TCP}}{d_{\beta TCP}}} \cdot d_{HAP} + \frac{\frac{MF_{\beta TCP}}{d_{\beta TCP}}}{\frac{MF_{HA}}{d_{HA}} + \frac{MF_{\beta TCP}}{d_{\beta TCP}}} \cdot d_{\beta TCP} \tag{5}$$

If the granules are manufactured by crushing porous blocks, the porosity of granules should be measured on the blocks before crushing by the method described above.

Otherwise, the porosity of granules should be estimated by mercury porosimetry.

4.4.2 Size of micropores and macropores

4.4.2.1 Micropores

To perform the metallographic cuts of the material, it can be necessary in some cases to perform an embedding of the material in a resin before cutting.

The diameter of micropores shall be specified. It shall be determined by measuring the diameter of micropores on SEM photomicrographs of a section of the material by applying one of the methods

described in ISO 13383-1 to micropores only. As for the part where pores are touching each other, draw a fictive boundary between the pores.

4.4.2.2 Macropores

4.4.2.2.1 General

The diameter of macropores shall be specified. The characterization can be performed either by method A or method B.

4.4.2.2.2 Method A: SEM

To perform the metallographic cuts of the material, it can be necessary in some cases to perform an embedding of the material in a resin before cutting.

Measure the diameter of macropores on SEM photomicrographs of a section of the material by applying one of the methods described in ISO 13383-1 to macropores only. As for the part where pores are touching each other, draw a fictive boundary between the pores.

4.4.2.2.3 Method B: Micro-focus CT analysis

Visual display of three-dimensional macroporous structure (pore shape, wall thickness, isotropy, homogeneity), macroporosity, and the distribution histogram of pore diameter can be determined by micro-focus CT analysis. The macroporosity shall be determined by measuring porosity of a field of view (FOV) of 3 mm in diameter by 1,5 mm in height in three-dimensional analysis of the micro-focus CT images. Average and standard deviation of the macroporosity of several FOVs shall be calculated. The pore diameter histogram shall be obtained by counting the number of the pores of each diameter range. Recommended spatial resolution is 6 µm/pixel. Recommended specimen size is 5 mm in diameter and 10 mm in height.

4.4.3 Interconnections

Macropores should be mainly opened and interconnected. Interconnections diameter between macropores shall be specified. It shall be determined by mercury porosimetry in accordance with ISO 15901-1.

The principle of this measure is to force mercury penetrating in the pores of the sample by applying a pressure more or less high. Low pressure allows penetration in high diameter interconnections and high pressure allows penetration in low diameter interconnections. The mercury volume that penetrated inside of the sample then corresponds to the volume of pores that can be reached thanks to interconnections (which size depends on the applied pressure).

The diameter of the interconnections of the main mercury penetration peak shall be determined. The volume of porosity accessible through interconnections with diameter higher than 5 µm shall be determined.

Micro-focus CT images including reconstructed 2- and/or 3-dimensional images could provide supplemental information about interconnection of macropores, especially for material with interconnections larger than 100 µm, when mercury porosimetry is limited.

if the tolerance for specifications on porosity is more than ± 2 % for blocks, the test shall be conducted on samples with the lower and the higher porosity.

4.5 Dissolution and pH change

The *in vitro* dissolution rate of bone substitute can be used to compare the ability of different bone substitutes to resorb *in vivo*, even if mechanisms different from dissolution will occur *in vivo*. Significant pH change after implantation can impair osteoconduction at the surface of the bone substitute. The aim of the following tests is to measure the *in vitro* dissolution rate of bone substitutes and pH change of the dissolution medium.

Dissolution and solubility of the device shall be tested. Three samples of bone substitute shall be introduced in three flasks of TRIS buffer solution at pH (7,3 ± 0,1) at (37 ± 1) °C. The three solution flasks shall be placed on a plate agitator with a rotation speed of 200 rpm for 24 h, 48 h and 72 h respectively. The dissolution rate shall be measured under the conditions of a constant ratio of initial material mass to total dissolution media volume. The ratio of test material mass to dissolution media volume shall be between 0,1 and 4,0 mg/ml.

pH shall be measured after 0 h, 24 h, 48 h and 72 h of immersion. pH shall not vary by more than 0,3 from the initial value during testing.

Calcium content of the solutions shall be analysed by ICP/AES or AAS or ICP/MS, or potentiometrically with an ion probe. The concentrations versus time curve shall be determined.

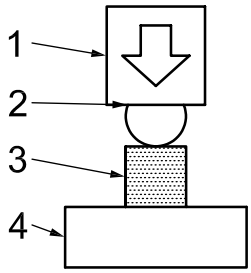
4.6 Measurement of material mechanical strength

4.6.1 General

Mechanical strength of the bone substitute in the form of blocks shall be assessed by a sphere indentation test (see Figure 1) and/or compressive strength test (see Figure 2).

For high porosity materials (total porosity ≥ 40 %), the mechanical strength of the bone substitute shall be assessed by a spherical indentation test.

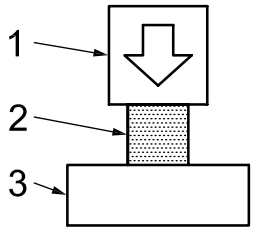
It is acceptable to use the compressive strength test instead of an indentation test for high porosity materials but the spherical indentation test was shown to be more reproducible in a round robin test for high porosity materials.



Key

1 piston
2 sphere
3 test specimen
4 pedestal

Figure 1 — Schematic drawing of the sphere indentation test



Key

1 piston
2 test specimen
3 pedestal

Figure 2 — Schematic drawing of the compressive strength test

For low porosity materials (<40 %), the mechanical strength of the bone substitute shall be assessed by a compressive strength test.

4.6.2 Apparatus, sampling and specimen

4.6.2.1 Apparatus

4.6.2.1.1 Test machine

A test machine shall be constructed so that compressive stress can be applied to a test specimen at a constant crosshead speed. The test machine shall be equipped with an apparatus recording the load with an accuracy of 1 % of the maximum load.

4.6.2.1.2 Sphere

A steel sphere with 9,52 mm diameter shall be used as an indenter.

4.6.2.1.3 Piston

For the compressive strength test, the piston applying the force to the specimen shall be made of steel having hardness 300 HV or higher (30 HRC or higher). The thickness of the piston shall be at least 10 mm, and the upper surface area of the piston is at least four times the specimen cross section area. The R_a roughness of the surface of the piston contacting with the specimen shall be at most 0,40 µm, and the parallelism shall be at most 0,01 mm.

For the spherical indentation test, the piston shall be designed so that the sphere is centred in the axis of the piston.

4.6.2.1.4 Pedestal

A pedestal placed below the specimen shall be made of steel having hardness 300 HV or higher (30 HRC or higher). The thickness of the pedestal shall be at least 10 mm, and the upper surface area of the pedestal is at least four times the specimen cross section area. The R_a roughness of the surface of the pedestal contacting with the specimen shall be at most 0,40 µm, and the parallelism shall be at most 0,01 mm.

4.6.2.2 Procedure

4.6.2.2.1 General

If the tolerance for specifications on porosity is more than ± 2 %, compressive strength shall be measured on samples with the lower and the higher porosity.

4.6.2.2.2 Soaking method

Calcium and magnesium free phosphate buffered saline [PBS(-)] shall be used as a soaking solution.

The specimen is deaerated by vacuum pump into an appropriate container placed on the vacuum chamber and PBS(-) is introduced into the specimen container. The amount of PBS(-) shall be at least 10 times greater than the apparent volume of the specimen. The standard degree of vacuum is (2 to 3) 10^3 Pa. The soaking time is (24 ± 1) h and temperature is (25 ± 3) °C. The moisture of the test specimen is wiped before the test.

In addition, the tests can be carried out under dry conditions.

4.6.2.2.3 Specimen positioning and loading method

The specimen is positioned at the centre of the pedestal. The central axis of the pedestal, specimen, sphere and piston are aligned along the load line.

The cross head speed shall be (0,50 ± 0,05) mm/min.

Load shall be recorded from the start of the test to the specimen fracture.

For the spherical indentation test, the size of indentation on the specimen shall be smaller than the diameter of the cylinder or the horizontal length and vertical length of the cube.

For the compressive strength test, the force is applied on the 10 mm x 10 mm surface if a rectangle parallelepiped is used (see 4.6.2.4.1).

4.6.2.2.4 Reuse of piston, pedestal and sphere

When the piston, pedestal and sphere are reused, it shall be checked that there are no dimples or flaws on the contact plane. If dimples or flaws exist on the contact plane and cannot be removed, the parts may not be reused.

4.6.2.3 Spherical indentation test

4.6.2.3.1 Sampling and specimen

The sample size shall be at least 10 specimens.

The shape and size of a test specimen shall usually be a right circular cylinder. The standard dimension of a cylinder specimen shall be (10,0 ± 0,1) mm in diameter and (10,0 ± 0,1) mm in height. However, the test specimen may also be a cube with standard edge dimensions of (10,0 ± 0,1) mm. The parallelism between the upper and lower surfaces of the specimen shall be not greater than 0,1 mm. The squareness between the upper and lower surfaces and side surface of the specimen shall be not greater than 0,1 mm.

The diameter or the square base diagonal of the test specimen shall be longer than 10 times the diameter of the biggest porosity of the specimen. When the dimensions are different from the standard one, they shall be stated in a report.

4.6.2.3.2 Test results

For the sphere indentation test, the load versus displacement curve shall be drawn from the start of the test to the fracture of the test specimen. The maximum load and the displacement at the maximum load from each load versus displacement curve shall be recorded.

The maximum load, P_{Si}, shall be the strength of the sphere indentation. The mean value and the standard variation of the strength of the sphere indentation shall be calculated according to Formulae (6) and (7) and shall be rounded off to significant figures.

$$\bar{P}_S = \frac{1}{n}\sum_{i=1}^{n} P_{Si} \tag{6}$$

$$SD_S = \sqrt{\sum_{i=1}^{n} \frac{(\bar{P}_S - P_{Si})^2}{n-1}} \tag{7}$$

where

$\bar{P}_S$ is the mean compressive load (N);

P_{Si} is the indentation load of each specimen (N);

SD_S is the standard deviation of the compressive load (N);

n is the number of specimens.

4.6.2.4 Compressive strength test

4.6.2.4.1 Sampling and specimen

The sample size shall be at least 10 specimens.

The test specimen shall usually be a right circular cylinder, (10,0 ± 0,1) mm in diameter and (15,0 ± 0,1) mm high. However, the specimen may also be a rectangular base squared parallelepiped with standard dimensions (10,0 ± 0,1) mm in length, (10,0 ± 0,1) mm in width, and (15,0 ± 0,1) mm in height. The parallelism between the upper and lower surfaces of the specimen shall be not greater than 0,1 mm. The squareness between the upper and lower surfaces and side surface of the specimen shall be not greater than 0,1 mm.

The diameter or the square base diagonal of the test specimen shall be longer than 10 times the diameter of the biggest porosity of the specimen. When the dimensions are different from the standard one, they shall be stated in a report.

4.6.2.4.2 Test results

For the compressive strength test, the load versus displacement curve shall be drawn from the start of the test to the fracture of the test specimen. The maximum load from each load versus displacement curve shall be recorded.

The maximum load, P_{Ci}, shall be used for calculation of the compressive strength, according to Formula (8).

$$\sigma_{Ci} = \frac{P_{Ci}}{A_i} \tag{8}$$

where

σ_{Ci} is the compressive strength of the i-specimen (Pa);

P_{Ci} is the maximum load in each test (N);

A_i is the compressive area of each specimen (m^2).

A_i is calculated according to Formula (9) for cylindrical specimens

$$A_i = \frac{\pi \cdot \delta_i}{4} \tag{9}$$

where

δ_i is the diameter of each test specimen (m);

or according to Formula (10) for parallelepiped specimens

$$A_i = a_i^2 \tag{10}$$

where

a_i is the edge of the square base of each test specimen (m).

The mean value and the standard variation of the compressive strength shall be calculated according to Formulae (11) and (12) and shall be rounded off to significant figures in accordance with ISO 80000-1.

$$\bar{\sigma}_C = \frac{1}{n}\sum_{i=1}^{n}\sigma_{Ci} \tag{11}$$

$$SD_C = \sqrt{\sum_{i=1}^{n}\frac{(\bar{\sigma}_C - \sigma_{Ci})^2}{n-1}} \tag{12}$$

where

$\bar{\sigma}_C$ is the mean compressive strength (Pa);

SD_C is the standard deviation of compressive strength (Pa);

n is the number of specimens.

4.7 Test report

A test report shall be made for each test or group of tests and shall include the following information:

a) test method;

b) references of the test specimens (name, reference, physical form of the specimen, dimensions when applicable, lot number);

c) number of specimens used for each test;

d) references and calibration of the testing apparatus;

e) name and certifications of the testing laboratory;

f) raw results;

g) calculation methods used;

h) final results and tolerances;

i) when alternative test methods are permitted in this part of ISO 13175, a statement of which test method has been used;

j) testing apparatus settings;

k) characteristics of the components used in combination with the testing apparatus (e.g. size of the cells used for mercury porosimetry, material of the piston, sphere and pedestal for mechanical tests);

l) supplier and lot number of the consumable used during the tests (e.g. PBS, buffer solution); any deviations to the methods described in this part of ISO 13175.

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[3] ISO 13485, *Medical devices — Quality management systems — Requirements for regulatory purposes*

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