DRAFT INTERNATIONAL STANDARD

ISO/DIS 18531

ISO/TC **150**/SC **1**

Secretariat: **DIN**

Voting begins on:
2015-06-22

Voting terminates on:
2015-09-22

Implants for surgery — Calcium phosphate bioceramics — Characterization of hardening bone paste materials

Titre manque

ICS: 11.040.40

Reference number
ISO/DIS 18531:2015(E)

ISO copyright office
Ch. de Blandonnet 8 • CP 401
CH-1214 Vernier, Geneva, Switzerland
Tel. +41 22 749 01 11
Fax +41 22 749 09 47
copyright@iso.org
www.iso.org

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.

The procedures used to develop this document and those intended for its further maintenance are described in the ISO/IEC Directives, Part 1. In particular the different approval criteria needed for the different types of ISO documents should be noted. This document was drafted in accordance with the editorial rules of the ISO/IEC Directives, Part 2. www.iso.org/directives

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. Details of any patent rights identified during the development of the document will be in the Introduction and/or on the ISO list of patent declarations received. www.iso.org/patents

Any trade name used in this document is information given for the convenience of users and does not constitute an endorsement.

For an explanation on the meaning of ISO specific terms and expressions related to conformity assessment, as well as information about ISO's adherence to the WTO principles in the Technical Barriers to Trade (TBT), see the following URL: Foreword - Supplementary information

The committee responsible for this document is ISO/TC 150, *Implants for surgery*, Subcommittee SC 1, *Materials*.

Implants for surgery — Calcium phosphate bioceramics — Characterization of hardening bone paste materials

1 Scope

This International Standard specifies methods for measuring the physicochemical characteristics of calcium phosphate ceramic bone cement materials, prepared from mixing powder and liquid agents as supplied by the manufacturer and used in artificial bones and similar applications.

2 Normative references

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

ISO 7500-1, *Metallic materials — Verification of static uniaxial testing machines — Part 1: Tension/compression testing machines — Verification and calibration of the force-measuring system*

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

3 Terms and definitions

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

3.1
calcium phosphate bone cement
mixture of calcium phosphate powder and a liquid agent that after hardening becomes artificial bone

3.2
setting
loss of fluidity and hardening of a bone cement produced by a chemical reaction

3.3
setting time
time required from the start of powdered agent and liquid agent blending until hardening of the cement

3.4
disintegration rate
weight ratio of the disintegrated portion of the cylinder to that of the whole cylinder of the bone cement, when the cylinder is immersed in the physiological saline before hardening

4 Apparatus

4.1 Analytical eletronic balance, with 1 mg, or greater resolution.

4.2 Plastic spatula, with a flat tip for kneading the bone paste. To ensure uniform kneading of bone paste, a plastic spatula used primarily in dentistry is recommended.

4.3 Cement mixing tablet, for kneading the bone paste. To ensure uniform kneading of bone paste, a cement mixing tablet used primarily in dentistry is recommended. General purpose kneading tools, such as knife or spatula are also required.

4.4 Adjustable incubator or thermostatic bath, with a capacity of mantaining the material at a controlled temperature of (37 ± 2) °C and a controlled humidity of 95 % and 100 %, used for hardening measurements (see Clause 6), for disintegration tests (see Clause 8) and for compression test (see Clause 9). Alternatively, for the dynamic compression test (see 8.3), a thermostatic jacket, with capacity of mantaining the container temperature at (37 ± 0,5) °C during testing can be used.

To create 95 % to 100 % relative humidity in the incubator, attach an auxiliary tray such that water extends into the bottom of the opening/closing apparatus. Place a mould packed with bone paste onto the auxiliary tray; any water submerging the bottom surface of the tray presents a problem. To maintain a state of elevated humidity, the entire incubator may also be placed in a thermostatic chamber.

4.5 Specimen mould, for hardening measurements (see Clause 6), with diameter between 7 mm and 15 mm, and height between 3 mm and 5 mm. The mould used may be a vinyl chloride, acrylic, Polytetrafluoroethylene (PTFE), or other such pipe cut to an appropriate size.

4.6 Gillmore needle apparatus, for hardening measurements (see Clause 6). Setting time shall be measured with a light needle arm.

NOTE 1 This selection is a criterion for the recommended time elapsed in bone paste kneading and filling procedures.

NOTE 2 There are two needle arms in the apparatus, light and heavy - the first, with a 2,12 mm diameter and 113,4 g mass, and the other, with a 1,06 mm diameter and 453,6 g mass. The light needle arm is intended to show early hardening behaviour, and the heavy type to show subsequent hardening behaviour.

4.7 Specimen preparing device for pH monitoring, plastic tube with inner diameter 8 mm to 9 mm and a piston extruder, as presented in Figure 1, for pH-monitoring (see Clause 7).

4.8 Separating sheet or plastic sheet, e.g. a vinyl sheet, approx. 0,2 mm thickness, allowing ready separation of the bone paste and extruders. For pH-monitoring (see Clause 7), with approximately from 7,5 mm to 8,5 mm diameter, according to the diameter of the piston producing specimens. For static disintegration test (see 8.2), with approximately 4 mm.

4.9 Sample moulding tool, with inner diameter 4,8 mm, comprising an outer tube and an extruder which produce a bone paste sample with dimensions of 4,8 mm diameter, 16,5 mm length, and approximately 0,3 mL volume, used for static disintegration test (see 8.2).

4.10 Plastic container, with a volume of approximately 50 mL and a 50 mm inner diameter, for sample immersion in static disintegration test (see 8.1).

4.11 Physiological saline, isotonic solution containing 9,0 g of NaCl per litre.

4.12 Stainless steel wire rack, with 0,5 mm wire diameter, 10 mesh, 2,0 mm grid, 2 mm to 4 mm height, for supporting sample in the plastic container bath (see 8.2).

4.13 Dryer or incubator, with capacity of mantaining the material at a controlled temperature of (65 ± 5) °C, used for disintegration tests (see Clause 8).

4.14 Sample mould, a cylindrical tube with an inner diameter of 8 mm to 9 mm and a length of 16 mm to 18 mm, used for dynamic disintegration tests (see 8.3).

NOTE A volumetric disposable syringe with the outer tube tip cut off may be used.

4.15 Dynamic disintegration device, comprising a closable container of glass or other such inert material, a motor, and a rotating axis and circular basket and a rotation adjuster. The container is a cylinder with a lip at the top and a semi-circular bottom, capacity of 1 L, height of 160 mm to 210 mm, and

inner diameter of 98 mm to 106 mm. The rotating axis and cylindrical bath shall be made from stainless steel (SUS316) or an equivalent inert material. Figure 4 presents an example of a rotating axis and basket. The rotation adjuster shall allow adjustment in a range of the specified rpm ± 4 %. In addition to smooth rotation of the rotating axis, shall be ensured that no shaking or vibration by the apparatus or from its environs develops. To prevent the sample from contacting the basket, a sinker made from acid-resistant wire or other mesh (see Figure 5) shall be used.

4.16 Polytetrafluoroethylene (PTFE) split mould, with a through-hole of 6 mm and a thickness of 12 mm for the manufacture of compression specimens, constructed as a two-part split mould, such as shown in Figure 6, with the two halves being secured by a clamp (see Clause 9).

4.17 Micrometre or calliper, to measure specimen diameter, used for compression test (see Clause 9).

4.18 Glass sheet, to scrape off the bone paste protruding from the through-hole of the Polytetrafluoroethylene (PTFE) split mould (4.16), used for compression test (see Clause 9).

4.19 Stainless steel vat or container, where the Polytetrafluoroethylene (PTFE) split mould (see 9.2.1) can be completely submersed in a water bath, used for compression test (see Clause 9).

4.20 Mechanical testing machine, used for compression test (see Clause 9), suitable for applying a compressive load of at least 1 kN at a nominal speed of (0,5 ± 0,1) mm/min and equipped to record the peak force applied to an accuracy of better than 1 %. Calibration of the force-measuring device shall be performed in accordance with ISO 7500-1.

5 Sample preparation method

Sample of bone cement shall be prepared according to the method specified by the manufacturer after acclimation of materials to an indoor ambient temperature (23 ± 2) °C, for at least 60 min, unless otherwise specified by the manufacturer.

In case such a method is not availble, the following method shall be used alternatively.

Use an analytical balance to weigh the powdered agent and liquid agent to a powder/liquid ratio specified by the producer. Follow Table 1 for powdered agent division ratios and kneading times, and use the plastic spatula to knead the material for 90 s in total. Place the powdered agent at the upper right of the mixing tablet and the liquid agent at the centre. Divide the powdered agent into approximate thirds and knead the first third with the liquid agent for 20 s. Then add one third of the powdered agent and knead the full two-thirds amount for 30 s. Add the last one-third, knead for 40 s, and complete kneading at a total of 90 s from the outset.

Table 1 — Powdered agent division ratios and kneading times

Step	Powder division ratio	Kneading time (sec.)
1	1/3	20
2	1/3	30
3	1/3	40

6 Setting Time

6.1 Sample preparation

When measuring setting time, at least 1,5 g of powdered agent shall be used. The cement shall be prepared as specified in Clause 5. Gather the kneaded bone cement in the centre of the cement mixing tablet, and use a plastic spatula with a flat tip to pack it into a mould (diameter: 7 mm to 15 mm, height

3 mm to 5 mm). When 2 min have elapsed from the start of kneading, place the material in an adjustable incubator at (37 ± 2) °C and (95 to 100) % relative humidity for curing. To create (95 to 100) % relative humidity in the incubator, attach an auxiliary tray such that water extends into the bottom of the opening/closing apparatus. Place a mould packed with bone cement onto the auxiliary tray; any water submerging the bottom surface of the tray presents a problem. To maintain a state of elevated humidity, the entire incubator may also be placed in a thermostatic chamber.

6.2 Measurement method

Remove the mould packed with the bone cement from the incubator at one minute accumulated time, lower the flat tip of a Gillmore needle apparatus (light) to the sample surface. If an impression is formed, return any non-hardened material to the incubator again. Repeat this procedure at one minute interval until resulting impression is not formed any more. Setting time is defined with the accumulated time by this point. Samples shall be prepared and measured one by one. The setting time is determined by five or more repetitions of this procedure.

6.3 Report

a) Sample name (may include Product name, batch/lot number etc.).

b) Paste preparation parameters (powdered agent weight, liquid agent weight).

c) Mould dimensions (inner diameter, height).

d) Measured temperature and humidity in incubator.

e) Number of specimens.

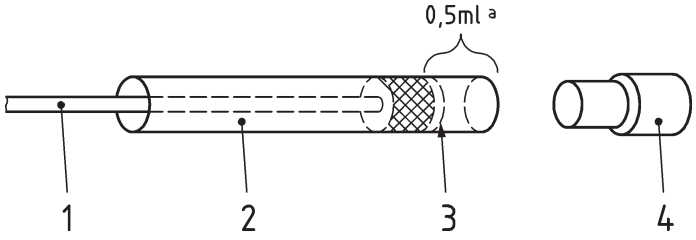
f) Setting time measurement results (mean, standard deviation).

g) Testing date, testing location, name of tester.

7 pH monitoring

7.1 Sample production method

Prepare the cement as specified in Clause 5 and the plastic tube with a separating sheet on the tip of the extruder as illustrated in Figure 1. The position of the extruder is adjusted so that volume to be filled is precisely 0,5 mL. Pack the cement into the plastic tube and remove the excess cement on the tip using a plastic spatula for smooth the surface.



Key

1 extruder
2 plastic tube
3 separating sheet
4 cap
a Volume of the bone cement sample.

Figure 1 — Schematic of the Specimen preparing device for pH monitoring

7.2 pH measurement

After 180 elapsed seconds from the start of kneading, use the extruder to immerse the bone cement on each separating sheet in 50 mL of distilled water at (37 ± 2) °C, and measure pH at 1 min, 10 min and 60 min after immersion.

Agitate the distilled water gently for 10 s before measurement of the pH, measure three specimens at least, and take the mean value as pH.

7.3 pH electrode calibration

When calibrating pH, perform two point calibration twice at a temperature of (37 ± 2) °C, with the electrode maintained at (37 ± 2) °C, using two standard pH buffer solutions of different pH.

7.4 pH measurement report

1) Sample name (may include Product name, batch/lot number etc.).

2) Paste preparation parameters (powdered agent weight, liquid agent weight).

3) Temperature of immersion bath.

4) pH measurement results (no. repetitions, mean, standard deviation).

5) Testing date, testing location, name of tester.

8 Disintegration rate

8.1 Type of testing

When bone cement transplanted into the body decomposes due to contact with bodily fluids, it is eroded by blood flow infiltrating from the margin of the transplantation site and may disintegrate. Consequently, two types of testing are specified: static disintegration testing, involving immersion in standing water, and dynamic disintegration testing, in which a sample is placed in a basket and rotated in a test solution to produce a dynamic state.

8.2 Static disintegration testing

8.2.1 Sample preparation

Gather the bone paste kneaded in accordance with Clause 5 in the centre of the cement mixing tablet, insert the appropriated separating sheet (4.8) into the sample mould (4.9) in advance and use the plastic spatula (4.2) to pack it into the outer tube of it. To prevent contamination by air bubbles at such time, position the extruder near the tip of the outer tube and withdraw the extruder in small increments while packing the bone paste. Complete the packing operation within three minutes from the start of kneading.

8.2.2 Procedure

Fill the approximately 50 mL plastic container (4.10) with 30 mL of physiological saline (4.11) and heat to (37 ± 2) °C in an incubator or thermostatic bath (4.4).

At five minutes from the start of kneading, as shown in Figure 2, use the filled sample mould to extrude the bone paste sample gently onto the centre of the stainless steel wire rack (4.12); then, as shown in Figure 3, gently place the rack holding the sample into the plastic container, immersing it in the physiological saline, and store for 72 h in a (37 ± 2) °C incubator.

The sample is thereby immersed completely in 30 mL of physiological saline, and any disintegrated bone paste drops off the wire rack.