



Standard Test Method for Evaluation of the Environmental Stability of Calcium Phosphate Coatings¹

This standard is issued under the fixed designation F 1926; the number immediately following the designation indicates the year of original adoption or, in the case of revision, the year of last revision. A number in parentheses indicates the year of last reapproval. A superscript epsilon (ε) indicates an editorial change since the last revision or reapproval.

1. Scope

1.1 This test method covers calcium phosphate coatings intended for use in surgical implant applications.

1.2 Aspects of the biological response to calcium phosphate materials in soft tissue and bone have been reported from laboratory studies and clinical use (1-10).²

1.3 The requirements of this specification apply to calcium phosphate coatings such as calcium hydroxyapatite (see Specification F 1185), beta-tricalcium phosphate (see Specification F 1088), and biphasic mixtures thereof with or without intentional addition of other minor components (<10 %).

1.4 The coating(s) shall be representative of that produced for sale. It shall have been produced and processed under standard manufacturing conditions.

1.5 The coatings may be applied to porous, nonporous, textured, and other implantable topographical substrate forms representative of the end-use product.

1.6 The calcium phosphate coating may constitute the only coating on a substrate or be one multiple coatings.

1.7 This test method is limited to the laboratory evaluation of the dissolution rate of a calcium phosphate coatings. No correlation of the results to *in vivo* performance is implied.

1.8 The values stated in both inch-pound and SI units are to be regarded separately as the standard. The values given in parentheses are for information only.

1.9 *This standard does not purport to address all of the safety concerns, if any, associated with its use. It is the responsibility of the user of this standard to establish appropriate safety and health practices and determine the applicability of regulatory limitations prior to use.*

2. Referenced Documents

2.1 ASTM Standards:

E 691 Practice for Conducting an Interlaboratory Study to Determine the Precision of a Test Method³

¹ This test method is under the jurisdiction of ASTM Committee F04 on Medical and Surgical Materials and Devices and is the direct responsibility of Subcommittee F04.13 on Ceramic Materials.

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² The boldface numbers given in parentheses refer to a list of references at the end of the text.

³ *Annual Book of ASTM Standards*, Vol 14.02.

F 1088 Specification for Beta-Tricalcium Phosphate for Surgical Implantation⁴

F 1185 Specification for Composition of Ceramic Hydroxyapatite for Surgical Implantation⁵

3. Terminology

3.1 Definitions of Terms Specific to This Standard:

3.1.1 *calcium phosphate*—any one of a number of inorganic chemical compounds containing calcium and phosphate ions as its principal constituents.

3.1.2 *coating*—a layer of material mechanically or chemically adhering to the surface of a substrate.

4. Dissolution Medium

4.1 Any water used for preparing reagents or dissolution medium shall be degassed carbon dioxide free deionized or distilled water and have less than 0.1 ppm each of residual Ca^{++} , phosphorus, and total solids.

4.2 *Unbuffered Water Medium*—Deionized or distilled water containing 8×10^{-5} M NaCl, 8×10^{-5} M CaCl_2 , and 5×10^{-5} M $\text{K}_3(\text{PO}_4)$.

4.3 *pH 5.5 MES Buffer Medium*—1.0 M MES, [2-(N-morpholino)ethanesulfonic acid] having a pH of 5.5 at $37 \pm 0.5^\circ\text{C}$ and containing 8×10^{-5} M NaCl, 8×10^{-5} M CaCl_2 , and 5×10^{-5} M $\text{K}_3(\text{PO}_4)$.

4.3.1 A buffer concentration of 1.0 M will usually provide sufficient buffer capacity to keep the solution within ± 0.1 pH units of the initial value. If this is not the case, the buffer capacity should be adjusted accordingly.

4.3.2 The pH must be adjusted to 5.5 at $37 \pm 0.5^\circ\text{C}$ using HCl or NaOH solutions.

4.4 *pH 7.4 TRIS Buffer Medium*—1.0 M TRIS, [Tris(hydroxymethyl)aminomethane] having a pH of 7.4 at $37 \pm 0.5^\circ\text{C}$ and containing 8×10^{-5} M NaCl, 8×10^{-5} M CaCl_2 , and 5×10^{-5} M $\text{K}_3(\text{PO}_4)$.

4.4.1 A buffer concentration of 1.0 M will usually provide sufficient buffer capacity to keep the solution within ± 0.1 pH units of the initial value. If this is not the case, the buffer capacity should be adjusted accordingly.

⁴ *Annual Book of ASTM Standards*, Vol 13.01.

⁵ Discontinued; See 2001 *Annual Book of ASTM Standards*, Vol 13.01.

4.4.2 The pH must be adjusted to 7.4 at $37 \pm 0.5^\circ \text{C}$ using HCl or NaOH solutions.

5. Analytical Parameters

5.1 The following procedure should be performed with each of the medium listed:

5.1.1 The dissolution rate shall be measured under the conditions of a constant ratio of initial coating mass (mg) to total dissolution medium volume (mL). The ratio of coating to dissolution medium shall typically be between 0.005 and 0.01 mg/mL.

5.1.2 The dissolved Ca^{++} concentration (± 1 ppm) and dissolved phosphorus (as P) concentration (± 1 ppm) shall be measured as soon as practical after the start of the experiment and at appropriate time intervals thereafter to allow the determination of their changes with time.

6. Analytical Procedures

6.1 Make pH measurements with an appropriately calibrated pH meter and probe.

6.2 Measure the Ca^{++} concentrations potentiometrically. Other methods (for example, colorimetrically, atomic absorption (AA), inductively coupled plasma (ICP) spectroscopy, or inductively coupled plasma mass spectroscopy (ICP/MS)) may be used if equivalency can be demonstrated.

6.3 Total phosphorus concentrations shall be measured by the phosphomolybdate complex method (11). Other methods (for example, inductively coupled plasma (ICP) spectroscopy or inductively coupled plasma mass spectroscopy (ICP/MS)) may be used if equivalency can be demonstrated.

6.4 An appropriate bacteriostat (for example, 0.1 v/v % Hibiclens or 0.1 w/v % sodium azide) may be added to the dissolution medium prior to the start of an experiment.

7. Dissolution Apparatus

7.1 The dissolution vessel (see Fig. 1) shall be of such design to easily accommodate the test specimen (see Fig. 2), the magnetic stirrer bar, and the specific ion-electrode and reference electrode assemblies. It shall also be isolated from the atmosphere by an oxygen and carbon dioxide free inert gas purge.

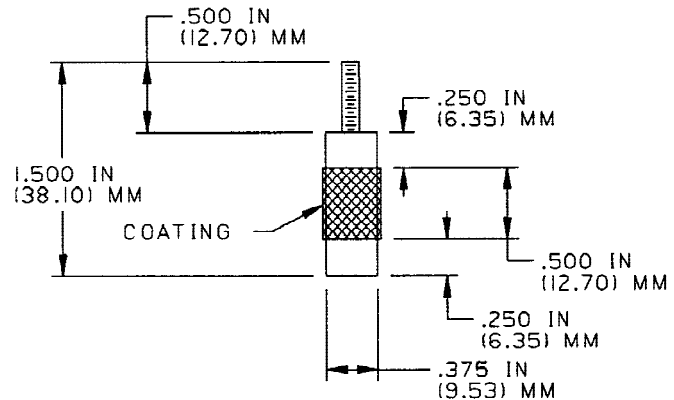


FIG. 2 Test Specimen and Coating

7.1.1 A convenient apparatus (see Fig. 1) is a 100 ml jacketed beaker⁶ with circulating water from a thermostatically controlled vessel. A flat piece of polyethylene, or other inert plastic, with appropriate holes drilled to accommodate the probes, sample holder, and purge gas tube can serve as a lid.

7.2 It shall be of appropriate dimensions to contain the required volume of dissolution medium at a level to facilitate sufficient stirring action from the magnetic stirrer bar.

7.3 The stirrer assembly shall be capable of maintaining a constant stirring rate of 100 ± 20 rpm.

7.3.1 *Magnetic stirrer bar*⁷—(0.31 in. (8 mm) diameter, 2 in. (51 mm) length, polytetrafluoroethylene (PTFE)-coated).

7.3.2 A different type of stirrer design and stirring rate may be used provided equivalence in experimental results can be demonstrated.

7.4 The dissolution vessel shall be thermostatically controlled at $37 \pm 0.5^\circ \text{C}$.

7.5 The dissolution apparatus may include various data recording and storage devices, strip chart recorders, computers,

⁶ Available from Ace Glass, P.O. Box 688, Vineland, NJ 08362-0688, catalog no. 5340.

⁷ Available from Fisher Scientific, 2000 Park Lane Dr., Pittsburgh, PA 15275, catalog no. 14-511-65, or equivalent.

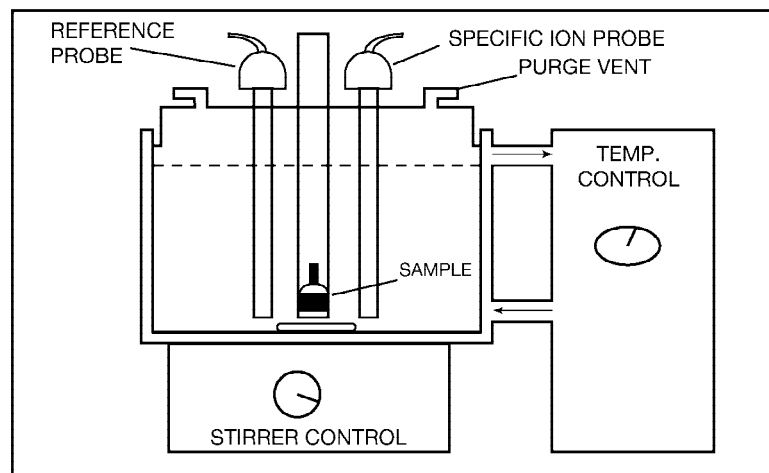


FIG. 1 Dissolution Apparatus

and so forth, to facilitate continuous monitoring throughout the duration of the experiment.

8. Preparation of Test Specimens

8.1 The standard test specimen for coating evaluation is defined in Fig. 2.

8.2 The test specimen shall be manufactured from the same materials and processes as substrates produced for sale.

8.3 The test specimen shall have the upper shank threaded so as to mate with an appropriate supporting shaft as described in Fig. 1.

8.4 By appropriate masking, or other techniques, the coating shall be applied only to the central 0.5 ± 0.005 in. of the test specimen.

8.5 The coating shall be applied to the test specimen and receive the same processing steps as the actual product.

9. Procedure for Monitoring Changes in pH, Calcium, and Phosphorus Concentrations

9.1 Prepare the test specimen as described in Section 8.

9.2 Procure the appropriate volume of dissolution medium needed for the experiment and equilibrate at 37 ± 0.5 °C.

9.3 Calibrate the pH probe, the ion-selective probes, and any other analytical instrumentation to be used immediately before starting the experiment as recommended by the manufacturers.

9.4 Adjust the stirrer assembly to 100 ± 20 rpm.

9.5 Assemble the dissolution apparatus (see Fig. 1). The dissolution medium, all calibrated sensing electrodes, and the stirrer should be in place and operating. However, do not include the test specimen. Then equilibrate this assembly at 37 ± 0.5 °C.

9.6 Record the initial pH of the test medium.

9.7 Set the experiment timing device to zero.

9.8 When ready to begin the experiment, add the test specimen to the stirrer and dissolution vessel. Start the timer and stirrer, and make any necessary adjustments to the equipment.

9.9 As soon as practical after the introduction of the test specimen to the dissolution medium, record the initial pH and the dissolved Ca^{++} and phosphorus concentrations.

9.10 Repeat the measurement of the pH, dissolved Ca^{++} , and dissolved phosphorus concentrations at appropriate time intervals to define their dissolution rate curves.

9.10.1 A typical initial sampling rate shall be every three minutes or more frequently for the first 15 min. More frequent sampling may be necessary for some materials in order to accurately determine the slope of the initial linear portion of the dissolution curve.

9.10.2 A typical final sampling rate shall be every hour or more frequently for the next 23 h of the experiment and then every 10 min for the last hour of the experiment.

9.10.3 If aliquots of the test solution are removed for subsequent testing during the course of the experiment, they shall be immediately replaced with an equal volume of fresh medium. If such replacements result in a discontinuity in the Ca^{++} or phosphorous concentration, a correction for the discontinuity shall be made in the reported results.

9.10.4 The duration of a typical experiment shall be at least 24 h. Longer times may be needed for some materials if their measured pH or concentrations of dissolved Ca^{++} or phosphorous continue to change by more than 10 % over a 3 h period.

10. Report

10.1 Report the following results for each of the medium systems used:

10.1.1 All procedural details that differ from those described in this test method.

10.1.2 The coating mass to dissolution volume ratio of the test.

10.1.3 The identity of the dissolution medium, the substrate material, and the mass to volume ratio used.

10.1.4 The pH and concentrations of dissolved Ca^{++} and phosphorus recorded at the start of the experiment (see 9.9).

10.1.5 The pH and concentrations of dissolved Ca^{++} and phosphorus at the end of the experiment.

10.1.6 Plots of the pH and concentrations of total dissolved Ca^{++} and phosphorus versus time data for the duration of the experiment.

10.1.7 The calculated initial dissolution rates (R_i) as follows:

10.1.7.1 Calcium phosphate coatings typically display two quasi-linear regions in their dissolution rate curves. The initial dissolution rate is usually distinguished from the final dissolution rate by a significantly higher rate of increase in the concentrations of dissolved Ca^{++} and phosphorus. The final dissolution rate is that rate observed immediately prior to the termination of the experiment.

10.1.7.2 The initial dissolution rate (R_i) of a coating is expressed in terms of the initial changes in total Ca^{++} or phosphorus concentrations with time:

$(R_i)_{\text{Ca}}$ = Initial slope of the Ca^{++} concentration versus time curve expressed in terms of the total dissolved Ca^{++} (in mg) per mg of coating per mL of dissolution medium per hour.

$(R_i)_\text{P}$ = Initial slope of the phosphorus concentration versus time curve expressed in terms of the total dissolved phosphorous (in mg) per mg of coating per mL of medium per hour.

10.1.8 The calculated final dissolution rates (R_f) as follows:

10.1.8.1 The final dissolution rate of a coating expressed in terms of the final changes in Ca^{++} and phosphorus concentrations:

$(R_f)_{\text{Ca}}$ = Final slope of the Ca^{++} versus time curve expressed in terms of the total dissolved Ca^{++} (in mg) per mg of coating per mL of dissolution medium per hour.

$(R_f)_\text{P}$ = Final slope of the phosphorus concentration versus time curve expressed in terms of the total dissolved phosphorous (in mg) per mg of coating per mL of medium per hour.

11. Precision and Bias

11.1 Precision and bias of this test method will be determined after interlaboratory tests are carried out and the results tabulated. The interlaboratory tests will be carried out following Practice E 691.

12. Keywords

12.1 calcium-phosphate ceramic; coating; dissolution rate; environmental stability

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