Designation: F1609 – 23

Standard Specification for Calcium Phosphate Coatings for Implantable Materials[1]

This standard is issued under the fixed designation F1609; 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 specification covers the material requirements for calcium phosphate coatings for surgical implant applications.

1.2 In particulate and monolithic form, the calcium phosphate materials system has been well characterized regarding biological response (**1**, **2**)[2] and laboratory characterization (**2-4**). Several publications (**5-10**) have documented the *in vitro* and *in vivo* properties of selected calcium phosphate coating systems.

1.3 This specification covers hydroxylapatite coatings, other calcium phosphate (for example, octacalcium calcium phosphate, amorphous calcium phosphate, dicalcium phosphate dihydrate) coatings, or a coating containing a combination of two or more calcium phosphate phases, with or without intentional minor additions of other elements or compounds (for example, fluorine, manganese, magnesium, carbonate),[3] and applied by methods including, but not limited to, the following: (*1*) plasma spray deposition, (*2*) solution precipitation, (*3*) dipping/sintering, (*4*) electrophoretic deposition, and (*5*) sputtering.

1.4 For a coating containing two or more calcium phosphate phases, one or more of which will be a major phase or major phases in the coating, while the other phase(s) may occur as a second or minor phases, the phase composition(s) of the coating should be determined against each corresponding crystalline phase, respectively. See X1.2.

1.5 Substrates may include smooth, porous, textured, and other implantable topographical forms.

1.6 This specification excludes organic coatings that may contain calcium and phosphate ionic species.

1.7 *This international standard was developed in accordance with internationally recognized principles on standardization established in the Decision on Principles for the Development of International Standards, Guides and Recommendations issued by the World Trade Organization Technical Barriers to Trade (TBT) Committee.*

2. Referenced Documents

2.1 *ASTM Standards:*[4]

E376 Practice for Measuring Coating Thickness by Magnetic-Field or Eddy Current (Electromagnetic) Testing Methods

F1044 Test Method for Shear Testing of Calcium Phosphate Coatings and Metallic Coatings

F1088 Specification for Medical-Grade Beta-Tricalcium Phosphate Raw Material for Implantable Medical Devices

F1147 Test Method for Tension Testing of Calcium Phosphate and Metallic Coatings

F1160 Test Method for Shear and Bending Fatigue Testing of Calcium Phosphate and Metallic Medical and Composite Calcium Phosphate/Metallic Coatings

F1185 Specification for Composition of Medical-Grade Hydroxylapatite for Surgical Implants

F1854 Test Method for Stereological Evaluation of Porous Coatings on Medical Implants

F1926 Test Method for Dissolution Testing of Calcium Phosphate Granules, Fabricated Forms, and Coatings

F2024 Practice for X-ray Diffraction Determination of Phase Content of Plasma-Sprayed Hydroxyapatite Coatings

2.2 *U.S. Pharmacopeia Convention Documents:*[5]

National Formulary XVI Tribasic Calcium Phosphate

USP <191> Chemical Tests—Calcium and Phosphorous

USP <211> Arsenic

USP <232> Elemental Impurities—Limits

USP <233> Elemental Impurities—Procedures

USP <251> Lead

USP <261> Mercury

[1] This specification 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.

Current edition approved July 1, 2023. Published July 2023. Originally approved in 1995. Last previous edition approved in 2014 as F1609 – 08 (2014). DOI: 10.1520/F1609-23.

[2] The boldface numbers in parentheses refer to the list of references at the end of this specification.

[3] The Joint Committee on Powdered Diffraction has established a Powder Diffraction File. The committee operates on an international basis and cooperates closely with the Data Commission of the International Union of Crystallinity and ASTM. Hydroxylapatite data can be found on file card No. 9-432; beta tricalcium phosphate data can be found on file card No. 9-169.

[4] For referenced ASTM standards, visit the ASTM website, www.astm.org, or contact ASTM Customer Service at service@astm.org. For *Annual Book of ASTM Standards* volume information, refer to the standard's Document Summary page on the ASTM website.

[5] Available from U.S. Pharmacopeia (USP), 12601 Twinbrook Pkwy., Rockville, MD 20852-1790, http://www.usp.org.

2.3 *Other Documents:*
U.S. Geological Survey Method Cadmium[6]
U.S. Code of Federal Regulations Title 21 (CFR 21), Part 820 Quality System Regulation[7]
X-Ray Diffraction Analyses[3]
ICH Q3D ICH Harmonized Guideline for Elemental Impurities[8]

3. Terminology

3.1 *Definitions:*

3.1.1 *amorphous calcium phosphate*—a non-crystalline calcium phosphate.

3.1.2 *beta tricalcium phosphate*—a calcium phosphate substance of empirical chemical formula, $Ca_3(PO_4)_2$ (see Specification F1088).

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

3.1.4 *coating*—a layer of mechanically or chemically attached material covering a substrate material.

3.1.5 *hydroxylapatite*—a calcium phosphate crystalline compound of empirical chemical formula, $Ca_5(PO_4)_3OH$ (see Specification F1185).

4. Chemical or Crystallographic Requirements, or Both

4.1 *Chemical:*

4.1.1 Elemental analysis for calcium and phosphorous and intentional additions (other than elemental impurities) shall be consistent with the expected stoichiometry of the specific calcium phosphate compound(s). The calcium and phosphorus content shall be determined using a suitable method such as USP <191> Identification Tests for Calcium and Phosphate, USP <232> Elemental Impurities—Limits, and USP <233> Elemental Impurities—Procedure (see 2.2) or X-ray fluorescence.

4.1.2 The analysis of elemental impurities may be required, based on the conditions, apparatus, or environments specific to the coating application technique used.

4.1.2.1 The significance of elemental impurities within an absorbable material is ultimately dependent on the dimensional characteristics of the final product and the rate of release of those initially interstitial elements into the surrounding tissue and extracellular fluid. Thus, any risk assessment of such impurities will be dependent on the final product design and intended application. More detailed and pharmaceutical-oriented guidance regarding the appropriate means for both monitoring and assessing relevant elemental impurities within a final product can be found in USP Chapters <232> and <233> and in the ICH Harmonised Guideline for Elemental Impurities—Q3D.

4.1.2.2 Determine the concentration of the respective elemental impurities within the coating by utilizing inductively coupled plasma mass spectroscopy (ICP-MS) or inductively coupled plasma atomic or optical emission spectroscopy (ICP-AES or ICP-OES) or an equivalent alternative method as described in Chapter <233> of the U.S. Pharmacopeia. The specific 24 different elemental impurities of interest are outlined in both USP <232> and in Table A.2.2 of the ICH Harmonised Guideline for Elemental Impurities—Q3D. Both of these documents include risk-based approaches toward the assessment and control of elemental impurities.

4.1.2.3 Except for intentionally added elements, assess the obtained results for compliance with the Parenteral Concentration limits described within the Individual Component Option of USP <232>, Table 3 (derived from ICH Q3D Option 1, Table A.2.2). If all listed elements except for those that are intentionally added can be assured to be maintained within the Parenteral Concentration Individual Component Option limits, the material "conforms" to the USP <232> elemental impurities limits (except for those intentionally added). If any listed element (other than those intentionally added) cannot be controlled to be maintained within the prescribed USP <232> limits, the material does not conform with the USP <232> elemental impurities limits and the concentration (in ppm, per USP <233> or equivalent) of each uncontrolled element shall be both monitored and reported.

4.1.2.4 The elemental impurities thresholds for the Individual Component Option of USP <232>, Table 3, provide specific elemental daily dosage limits for parenteral drug products. These daily elemental impurity limits (including those applied to intentionally added elements) should be considered as conservative thresholds for informational purposes only when applied to absorbable implants. Proper application of these limits in setting material specifications should consider the amount of the coating in the final implant product as well as its degradation and elemental elution rate into the surrounding tissue.

4.1.2.5 The elemental impurity content of the coating used in implants with a successful clinical history may also be considered in setting limits for material specifications. For such data to be relevant, analyses shall be consistent with the methods of USP <233> and shall be conducted on raw material lots used for clinically released product.

4.1.3 The analysis of intentional additional elements or compounds such as fluorine, manganese, magnesium, carbonate, and so forth shall be specified (concentration in ppm, per USP <233> or equivalent) for calcium phosphate coatings.

4.1.4 Calcium to phosphorus ratio (Ca/P) shall be performed on both the powder and coating forms using a suitable method.

4.2 *Crystallographic Characterization:*

4.2.1 Crystallographic characterization shall be in accordance with Practice F2024.

[6] Crock, J. G., Felichte, F. E., and Briggs, P. H., "Determination of Elements in National Bureau of Standards Geological Reference Materials SRM 278 Obsidian and SRM 688 Basalt by Inductively Coupled Argon Plasma—Atomic Emission Spectrometry," *Geostandards Newsletter*, Vol 7, 1983, pp. 335–340.

[7] Available from Standardization Documents Order Desk, DODSSP, Bldg. 4, Section D, 700 Robbins Ave., Philadelphia, PA 19111-5098, http://dodssp.daps.dla.mil.

[8] Available from International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH), ICH Secretariat, Route de Pré-Bois, 20, P.O Box 1894, 1215 Geneva, Switzerland, https://www.ich.org.

4.2.2 Testing shall include quantitative phase analysis and amorphous calcium phosphate content.

4.2.3 FTIR (Fourier Transform Infrared Spectroscopy) shall be performed to identify functional groups.

4.3 *Environmental Stability*—Environmental stability testing shall be performed in accordance with Test Method F1926 to assess the relative dissolution behavior of the material.

4.4 It is recommended that all metals or oxides present in concentrations equal or greater than 0.1 % be noted in material descriptions.

5. Physical Characterization

5.1 *Coverage of Substrate:*

5.1.1 Microscopic examination of the surface will be made at 10× magnification; "bare" areas, "pinholes," cracking, foreign debris, unmelts, chips, delamination and the appearance at the coating/substrate interface, and so forth shall be reported.

5.2 *Thickness*—The thickness shall be measured from cross sections in accordance with Test Method F1854. If distinct layers exist, they should be reported.

5.2.1 Alternatively, a magnetic field or eddy current technique (Practice E376) may be used if it has been shown to be equivalent to Test Method F1854.

5.3 *Porosity*—The porosity and pore size characterization shall be determined in accordance with Test Method F1854. This characterization may not be applicable to some calcium phosphate coatings (for example, a dense coating with a thickness of several micrometers), and in these situations, other test methods such as scanning electron microscopy (SEM), micro-computed tomography (uCT), or mercury (Hg) porosimetry may be considered as appropriate if a proper rationale is provided.

5.4 *Color*—A macroscopic examination (visual inspection) of color should be performed to guarantee a uniform and consistent appearance, in consideration of the specific process, substrate material and geometry, and coating thickness.

5.5 *Surface Topography*—The surface topography shall be measured using equipment designed to determine surface roughness. Characterization of the surface topography of the underlying substrate may be required, if applicable, for the specific coating method. Scanning electron microscopy shall be used to provide a visual representation of the coating surface characteristics.

6. Mechanical Characterization

6.1 The following mechanical characterizations may be applicable to a coating, depending on the substrate material or geometry, coating thickness or location, or coating method(s). Characterization reports shall contain sufficient information regarding the test techniques, procedures, and standards used and details such as specimen orientation and proportional depth of thickness in order to represent the analysis accurately.

6.1.1 The tensile bond strength of the coating to the substrate shall be determined using Test Method F1147.

6.1.2 The shear strength shall be determined using Test Method F1044.

6.1.3 The fatigue strength shall be determined using Test Method F1160. Both the coating/substrate interface and the effect on the substrate should be evaluated. The effect of the coating on the resulting fatigue strength of an actual device should also be considered.

7. Test Specimen Fabrication

7.1 All test specimens for coating characterizations shall be prepared from coating lots and samples from the same production feedstock lots and prepared on the same equipment used to apply the coating to actual devices.

7.2 For device characterization, all test specimens should be subjected to the same processing and sterilization as the finished device, if applicable.

8. Contact with Calcium Phosphate Coatings

8.1 In general, extra precautions should be taken when handling calcium phosphate coatings.

8.1.1 Contact with the coatings should be limited to soft, biocompatible polymers.

8.1.2 The only solvents to come in contact with the coating shall be distilled water and high-purity isopropyl alcohol.

8.1.2.1 pH is critical, and should measure 7.0 or higher in any liquid that comes in contact with the coating.

8.1.3 Powder-free nitrile gloves shall be the only gloves used for handling coatings.

9. Quality Program Requirements

9.1 The manufacture of calcium phosphate coatings shall conform to the applicable FDA and ISO quality standards.

10. Keywords

10.1 bone implant; calcium phosphate; coating; dental implant; hydroxylapatite; mechanical tests; orthopedic medical devices; physical characterizations; tricalcium phosphate