Designation: F 2224 – 03

Standard Specification for High Purity Calcium Sulfate Hemihydrate or Dihydrate for Surgical Implants[1]

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1. Scope

1.1 This specification covers material requirements for unfabricated and fabricated forms of hydrated calcium sulfate intended for surgical implants. Fabricated forms may include pressed and cast surgical implants in various geometric shapes. The calcium sulfate hemihydrate in the unfabricated form can be converted with the addition of water or other water-containing solutions to a fabricated calcium sulfate dihydrate form.

1.2 The requirements of this specification apply to calcium sulfate combined with two molecules of water or two calcium sulfate molecules sharing one water molecule.

Approximate chemical formulae:

Calcium Sulfate Dihydrate
$CaSO_4 \cdot 2H_2O$

Calcium Sulfate Hemihydrate
$CaSO_4 \cdot 1/2H_2O$ or $CaSO_4 \cdot H_2O \cdot CaSO_4$

1.3 This specification specifically excludes calcium sulfate anhydrite and calcium sulfate forms that contain additives such as reinforcing phases, medicaments, biological agents, and so forth.

1.4 The presence of processing aids does not exclude a product from the physical and mechanical requirements of this specification.

1.5 Some provisions of Specification C 59/C 59M and Test Methods C 472 apply. Special requirements that are detailed in this specification are included to characterize the material which will be used in surgical implants.

1.6 The biological response to calcium sulfate in bone tissue has been well characterized by a history of clinical use **(1-14)**[2] and by laboratory studies **(15-18)**.

1.7 The following precautionary caveat pertains only to the test method portion, Sections 4, 5, and 6, of this specification. *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 requirements prior to use.*

2. Referenced Documents

2.1 *ASTM Standards:*

C 59/C 59M Specification for Gypsum Casting Plaster and Gypsum Molding Plaster[3]

C 472 Test Methods for Physical Testing of Gypsum, Gypsum Plasters and Gypsum Concrete[3]

F 648 Specification for Ultra-High-Molecular-Weight Polyethylene Powder and Fabricated Form for Surgical Implants[4]

F 756 Practice for Assessment of Hemolytic Properties of Materials[4]

F 763 Practice for Short-Term Screening of Implant Materials[4]

F 813 Practice for Direct Contact Cell Culture Evaluation of Materials for Medical Devices[4]

F 895 Test Method for Agar Diffusion Cell Culture Screening for Cytotoxicity[4]

F 981 Practice for Assessment of Compatibility of Biomaterials for Surgical Implants with Respect to Effect of Materials on Muscle and Bone[4]

F 1088 Specification for Beta-Tricalcium Phosphate for Surgical Implantation[4]

F 1635 Test Method for In Vitro Degradation Testing of Poly(L-lactic acid) Resin and Fabricated Form for Surgical Implants[4]

2.2 *Other Documents:*

BS 6463-102: 2001 Quicklime, Hydrated Lime and Natural Calcium Carbonate—Part 102: Methods for Chemical Analysis[5]

US Pharmacopeia XXIV (USP 24) NF-19[6]

[1] This specification is under the jurisdiction of ASTM Committee F04 on Medical and Surgical Materials and Devicesand is the direct responsibility of Subcommittee F04.13on Ceramic Materials.

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

[3] *Annual Book of ASTM Standards*, Vol 04.01.

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

[5] Available from the British Standards Institution, c/o IHS Engineering/IHS International, 15 Inverness Way East, Englewood, CO 80112.

[6] Available from U.S. Pharmacopeia (USP), 12601 Twinbrook Pkwy., Rockville, MD 20852.

CFR Title 21, Part 820 Quality System Requirements[7]
Food Chemical Codex (FCC)[8]
European Pharmacopeia[9]
ISO 10993-1 Biological Evaluation of Medical Devices[10]

3. Terminology

3.1 *Definitions:*

3.1.1 *calcium sulfate anhydrite*—a chemical substance having approximate molecular formula of $CaSO_4$.

3.1.2 *calcium sulfate dihydrate*—a chemical having the approximate molecular formula of $CaSO_4 \cdot 2H_2O$. This substance is also known as gypsum.

3.1.3 *calcium sulfate hemihydrate*—a chemical substance having approximate molecular formula of $CaSO_4 \cdot 1/2H_2O$ or $CaSO_4 \cdot H_2O \cdot CaSO_4$. The mineral name of this substance is bassanite and the substance is also known as Plaster of Paris in the clinical literature.

3.1.4 *processing aids*—any constituent intentionally used in the processing of the raw material to fulfill a certain technological purpose during treatment or processing, which may result in the unintentional but technically unavoidable presence of residues of the substance or its derivatives in the final product (<5 % by weight), provided that these residues do not present any health risk. Some examples would be: binders, lubricants, compaction aids, disintegrants, plasticizers, deflocculants, wetting agents, water retention agents, antistatic agents, antifoam agents, foam stabilizers, chelating or sequestering agents, phase stabilizers, and so forth.

4. Chemical Requirements

4.1 Calcium sulfate for surgical implants (raw material) shall have a purity of not less than 98 % for calcium sulfate (absent of water) when measured by USP 24 NF 19. (This purity measurement method may not be applicable to the fabricated forms containing substantial additives.)

4.2 The concentration of trace elements in the calcium sulfate raw material shall be limited to less than 10 ppm of total heavy metals (for example, arsenic, cadmium, mercury, and lead). Other metallic elements, such as iron, may also affect implant performance and should be kept to a minimum. For example, for calcium sulfate to meet USP grade, iron concentration should not be higher than 100 ppm. Methods for measuring these trace elements are described in Specification F 1088 (Coupled Plasma—Atomic Absorption Spectrometry), the United States Pharmacopeia (USP), European Pharmacopeia, or Food Chemical Codex (FCC). A second method that may be used to analyze acid insoluble impurities is described in BS 6463-102.

5. Physical and Mechanical Characterization

5.1 The following physical and mechanical characterization may be applicable to calcium sulfate for surgical implant applications in either the fabricated form or intra-operative fabricated form. When characterization test results are reported in labeling, the test methods associated with these results shall be referenced. Labeling can be defined as but is not limited to the product label, brochures, technical monographs, and other related documentation.

5.2 *Set Time*—If set time is an applicable property, it should be reported along with the method by which it was determined in order to inform the final user. The set time is defined as the typical time for the development of an implantable surgical implant. Test Methods C 472 as described in Specification C 59/C 59M can be used to define a typical set time. The actual method used for set time determination shall be described or referenced in labeling.

5.3 *Compressive Strength*—Calcium sulfate dihydrate in a fabricated final form is intended to be used in non-load bearing applications. If applicable to implant performance, documentation of typical compressive strength and the methods used to determine it should be reported in order to inform the final user. Test Methods C 472 as described in Specification C 59/C 59M can be used for the typical compression strength determination. The actual method used shall be described or referenced in labeling.

5.4 In vitro *Degradation*—For calcium sulfate dihydrate in a fabricated final form, weight loss from dissolution may be reported. If reported, the method used should be described or referenced.

6. Test Specimen Fabrication

6.1 Prepare test specimens from the same batch of material and by similar processes to those employed in fabricating the implant device.

7. Quality Program Requirements

7.1 The manufacturer shall conform to Good Manufacturing Practices (see Title 21, part 820, of the Code of Federal Regulations) or its equivalent.

8. Keywords

8.1 bone; calcium sulfate; gypsum; implant; plaster

[7] Available from U.S. Government Printing Office Superintendent of Documents, 732 N. Capitol St., NW, Mail Stop: SDE, Washington, DC 20401.

[8] Available from National Academy Press, 500 Fifth St., NW, Lockbox 285, Washington, DC 20055.

[9] Available from EDQM, European Pharmacopeia, Council of Europe, B.P. 907, F-67029, Strasbourg, France.

[10] Available from American National Standards Institute (ANSI), 25 W. 43rd St., 4th Floor, New York, NY 10036.