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Standard Specification for Ultra-High Molecular Weight Polyethylene Powder Blended With Alpha-Tocopherol (Vitamin E) and Fabricated Forms for Surgical Implant Applications[1]

This standard is issued under the fixed designation F2695; 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 ultra-high molecular weight polyethylene (UHMWPE) powder blended with alpha-tocopherol (Vitamin E) intended for use in surgical implants.

1.2 The requirements of this specification apply to alpha-tocopherol-containing UHMWPE in two forms. One is virgin polymer powder blended with alpha-tocopherol prior to consolidation (Section 4). The second is any form fabricated from this blended, alpha-tocopherol-containing powder from which a finished product is subsequently produced (Section 5). This specification does not apply to finished or semi-finished products that are doped with Vitamin E after consolidation.

1.3 Aside from blending with alpha-tocopherol, the provisions of Specifications F648 and D4020 apply. Special requirements detailed in this specification are added to describe powders containing alpha-tocopherol that will be used in surgical implants. This specification addresses material characteristics and does not apply to the packaged and sterilized finished implant. This specification also does not apply to UHMWPE materials extensively crosslinked by gamma and electron beam sources of ionizing radiation.

1.4 The following precautionary caveat pertains only to the fabricated forms portion, Section 5, 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, health, and environmental practices and determine the applicability of regulatory limitations prior to use.*

1.5 *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:*[2]

D648 Test Method for Deflection Temperature of Plastics Under Flexural Load in the Edgewise Position

D790 Test Methods for Flexural Properties of Unreinforced and Reinforced Plastics and Electrical Insulating Materials

D1898 Practice for Sampling of Plastics (Withdrawn 1998)[3]

D4020 Specification for Ultra-High-Molecular-Weight Polyethylene Molding and Extrusion Materials

F619 Practice for Extraction of Materials Used in Medical Devices

F648 Specification for Ultra-High-Molecular-Weight Polyethylene Powder and Fabricated Form for Surgical Implants

F748 Practice for Selecting Generic Biological Test Methods for Materials and Devices

F749 Practice for Evaluating Material Extracts by Intracutaneous Injection in the Rabbit

F756 Practice for Assessment of Hemolytic Properties of Materials

F763 Practice for Short-Term Screening of Implant Materials

F813 Practice for Direct Contact Cell Culture Evaluation of Materials for Medical Devices

F895 Test Method for Agar Diffusion Cell Culture Screening for Cytotoxicity

F981 Practice for Assessment of Compatibility of Biomaterials for Surgical Implants with Respect to Effect of Materials on Muscle and Insertion into Bone

2.2 *ISO Standards:*

ISO 3451–1 Plastics—Determination of Ash, Part 1: General Methods[4]

[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 F04.11 on Polymeric Materials.

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[2] 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.

[3] The last approved version of this historical standard is referenced on www.astm.org.

[4] Available from American National Standards Institute (ANSI), 25 W. 43rd St., 4th Floor, New York, NY 10036, http://www.ansi.org.

ISO 10993 Biological Evaluation of Medical Devices, Parts 1–12[4]

3. Terminology

3.1 *Definitions of Terms Specific to This Standard:*

3.1.1 *crosslinking*—the process by which ionizing irradiation produces chemical bonds between UHMWPE molecules.

3.1.2 *extensively crosslinked UHMWPE*—UHMWPE material that has been subjected to total doses of gamma and/or electron beam ionizing irradiation greater than 40 kGy.

3.1.3 *fabricated form*—any bulk shape of UHMWPE, fabricated from the virgin polymer powder, used during the process of fabricating surgical implants prior to crosslinking, packaging, and sterilization. A fabricated form includes a semi-finished rod or sheet as well as a direct compression molded component.

3.1.4 *generic property*—that property which is determined solely by the chemical composition and structure of the virgin polymer.

3.1.5 *ionizing irradiation*—gamma ray or high-energy electron irradiation sources.

3.1.6 *virgin polymer powder*—the initially delivered form of the polymer as synthesized from its monomers prior to any processing or fabrication into a medical device. The provided resin is typically in the form of pellets, granules, or powder and is the material from which fibers, tubes, rods, slabs, sheets, films, or specific parts and devices are fabricated. Specifically, it is the form of UHMWPE as obtained from the powder manufacturer and prior to blending and fabrication into a bulk shape.

4. Alpha-Tocopherol-Blended UHMWPE Powder Requirements

4.1 *Generic Properties:*

4.1.1 The virgin polymer shall be a homopolymer of ethylene in accordance with Specification D4020.

4.1.2 The resin type and solution viscosity number requirements are listed in Table 1 of Specification F648.

4.1.3 To promote uniformity between different lots of the virgin polymer powder, concentration limits for trace elements have been established and are listed in Table 1 of Specification F648.

4.1.4 When determined as described in ISO 3451–1, the mean ash of duplicate samples shall not exceed the limits established in Table 1 of Specification F648.

4.2 *Nongeneric Properties:*

4.2.1 When a 300 g sample is prepared and viewed in accordance with section 7.1.2 of Specification F648, there shall be no more particles of extraneous matter than that specified in Table 1 of Specification F648.

4.3 *Compositional Requirements:*

4.3.1 Only alpha-tocopherol (certified pharmaceutical grade) is to be blended with the virgin polymer powder.

4.3.1.1 The alpha-tocopherol content in the blended powder may be based on agreement between the vendor and purchaser.

4.3.1.2 When measured based on agreement between the vendor and purchaser, the alpha-tocopherol content added to the powder shall be reported in units of ppm and percent mass.

4.3.1.3 Uniformity of the alpha-tocopherol in the blended powder shall be measured based on agreement between the vendor and the purchaser.

4.3.1.4 No other stabilizers or processing aids are to be added to the virgin polymer powder.

5. Alpha-Tocopherol-Blended UHMWPE Fabricated Form Requirements

5.1 *Compositional Requirements:*

5.1.1 Only alpha-tocopherol-blended powder, specified in Section 4, is to be used to produce the fabricated form.

5.1.1.1 The alpha-tocopherol content in the fabricated form may be based on agreement between the vendor and purchaser.

5.1.1.2 When measured based on agreement between the vendor and purchaser, the alpha-tocopherol content used to produce the fabricated form shall be reported in units of ppm and percent mass.

5.1.2 Uniformity of the alpha-tocopherol in the fabricated form shall be measured based on agreement between the vendor and the purchaser.

5.1.3 No other stabilizers or processing aids are to be added to the alpha-tocopherol-blended polymer powder during manufacture of the fabricated form.

5.2 *Physical Requirements:*

5.2.1 *Foreign Matter Requirements:*

5.2.1.1 When 3200 cm^2 is evaluated according to section 7.2.2 of Specification F648, there shall be no more than ten particles of extraneous matter visible on the surface when visually inspected by normal or corrected vision.

5.2.2 *Morphology Requirements:*

5.2.2.1 When evaluated according to Annex 2 of Specification F648, the calculated Morphology Index (MI) shall be reported.

5.3 *Mechanical Requirements:*

5.3.1 UHMWPE in fabricated form from which implants shall be made shall meet the requirements listed in Table 2 of Specification F648.

5.3.2 The following mechanical tests may be conducted based on agreement between the vendor and purchaser: (*1*) deflection temperature; Test Method D648 (1.8 MPa); (*2*) flexural modulus; Test Methods D790 (secant, 2 % offset).

6. Sampling

6.1 Where applicable, the requirements of this specification shall be determined for each lot of powder and fabricated form by sampling sizes and procedures according to Practice D1898, or as agreed upon between the purchaser and seller.

7. Biocompatibility

7.1 No known surgical implant material has ever been shown to be completely free of adverse reactions in the human

body. However, published studies (**1-5**)[5] of specific formulations of alpha-tocopherol doped UHMWPE have shown that an acceptable level of biological response can be expected, as further discussed in X1.5. Virgin (undoped) UHMWPE has been shown to produce a well-characterized level of biological response following long-term clinical use. The clinical history for virgin UHMWPE indicates an acceptable level of biological response in the applications in which the undoped material has been utilized. When new applications of the material, or modification to the material or physical forms of the materials are being contemplated (such as, blending with alpha-tocopherol), the recommendations of ISO 10993, Parts 1–12 and Practice F748 should be considered and testing considered as described in Practices F619, F749, F756, F763, F813, and F981 as well as Test Method F895.

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

8. Keywords

8.1 alpha-tocopherol; fabricated forms; powdered form; ultra-high molecular weight polyethylene; vitamin E

APPENDIX

(Nonmandatory Information)

X1. RATIONALE

X1.1 This specification is intended to describe the properties required and the procedures to be followed in testing unirradiated raw materials of UHMWPE blended with alpha-tocopherol for medical implant applications. This specification does not purport to address the testing that is needed for implants that are fabricated from the raw materials specified herein.

X1.2 Alpha-tocopherol is a biocompatible stabilizer of polyolefins (**1-6**) and is intended to reduce oxidative degradation during processing, radiation processing, shelf life storage, and *in-vivo* exposure of UHMWPE. Several laboratory studies have demonstrated that alpha-tocopherol will stabilize irradiated UHMWPE from accelerated aging conditions intended to simulate a variety of severe oxidative challenges (**7-12**). Human clinical use of implants fabricated from alpha-tocopherol blended UHMWPE is reported to have begun in 2004. At present, the extent to which alpha-tocopherol will help stabilize UHMWPE implants from *in-vivo* oxidation has not yet been determined.

X1.3 While beneficial for oxidative stability, levels of alpha-tocopherol ≥1000 ppm may later interfere with subsequent radiation crosslinking steps (**7, 10**) during subsequent stages of the implant manufacturing process. With 1000 ppm of alpha-tocopherol, Oral et al. have reported an average reduction of 17 % in crosslink density following a dose of 100 kGy (**7**). On the other hand, levels of alpha tocopherol in the range 125 to 500 ppm appear to be effective for stabilization of UHMWPE, although the level of stabilization depends upon the dose of radiation and the type of oxidative challenge (**7, 11, 12**). Thus, crosslinking will be a function of both the alpha-tocopherol content and the radiation dose, both of which may depend upon the choice of the manufacturer. Consequently, this standard is not intended to specify a minimum alpha-tocopherol content for unirradiated raw materials that will subsequently be used to fabricate orthopedic implants. Device testing is recognized to be crucial for UHMWPE implants, but is beyond the scope of this standard specification.

X1.4 The current standard specifies alpha-tocopherol content to be reported based on the mass percentage of antioxidant blended with the virgin resin powder prior to consolidation. Experimental techniques, including Fourier transform infrared spectroscopy and high-performance liquid chromatography (HPLC) (**4, 7**), have been proposed in the literature for characterizing the content of alpha-tocopherol, and its by-products, in consolidated UHMWPE. At present these research techniques have not been standardized. In the future, when quantification techniques for UHMWPE containing alpha-tocopherol have been standardized, it is expected that the current specification will be updated to include more specific details regarding appropriate test methodologies.

X1.5 There is some limited biocompatibility regarding cytotoxicity, genotoxicity, and animal studies designed to evaluate the potential transformation products of Vitamin E following consolidation and radiation of blended UHMWPE biomaterials (**1, 2, 4**). These studies were performed using 8000 ppm blended UHMWPE (GUR 1020), which was irradiated with 25 kGy (**1, 2, 4**), which results in the equivalent, and more voluminous, transformation products as 1,000 blended UHMWPE irradiated with 200 kGy. However, additional biocompatibility testing in accordance with ISO 10993 may be necessary in order to fully address the biocompatibility of degradation products of alpha-tocopherol: (*1*) genotoxicity testing in a mammalian test system capable of detecting gene level and chromosome level mutations; (*2*) irritation sensitization testing; and (*3*) chronic toxicity and carcinogenicity testing. Additional testing to address the effect degradation products of alpha-tocopherol on particulate mediated inflammatory response may also be required.

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