Designation: F 763 – 99

Standard Practice for Short-Term Screening of Implant Materials[1]

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1. Scope

1.1 This practice provides guidelines for short-term testing or screening of candidate materials, both porous and dense, as to the effects of the material on animal tissue in which it is implanted. This is a rapid screening prodedure for determining acceptability of candidate materials.

1.2 This practice, along with other appropriate biological tests (including other appropriate ASTM tests) may be used in the biocompatibility assessment of the candidate materials for use in the fabrication of devices for clinical application.

1.3 This experimental protocol is not designed to provide a comprehensive assessment of the systemic toxicity, carcinogenicity, teratogenicity, or mutagenicity of the material since other standards deal with these issues.

1.4 This practice is one of several developed for the assessment of the biocompatibility of materials. Practice F 748 provides guidance for the selection of appropriate methods for testing materials for a specific application.

2. Referenced Documents

2.1 *ASTM Standards:*

F 75 Specification for Cast Cobalt-Chromium Molybdenum Alloy for Surgical Implant Applications[2]

F 86 Practice for Surface Preparation and Marking of Metallic Surgical Implants[2]

F 90 Specification for Wrought Cobalt-Chromium-Tungsten-Nickel Alloy for Surgical Implant Applications[2]

F 136 Specification for Wrought Titanium- 6 Aluminum–4 Vanadium 4V ELI (Extra Low Interstiitial) Alloy (UNS R56401) for Surgical Implant Applications[2]

F 138 Specification for Wrought 18 Chromium–14 Nickel–2.5 Molybdenum Stainless Steel Bar and Wire for Surgical Implants (UNS S31673)[2]

F 562 Specification for Wrought Cobalt-35 Nickel-20 Chromium-10 Molybdenum Alloy for Surgical Implant Applications[2]

F 563 Specification for Wrought Cobalt-Nickel-Chromium-Molybdenum-Tungsten-Iron Alloy for Surgical Implant Applications[2]

F 603 Specification for High-Purity Dense Aluminum Oxide for Surgical Implant Application[2]

F 648 Specification for Ultra-High-Molecular-Weight Polyethlene Powder and Fabricated Form for Surgical Implants[2]

F 748 Practice for Selecting Generic Biological Test Methods for Materials and Devices[2]

F 981 Practice for Assessment of Compatibility of Biomaterials for Surgical Implants with Respect to Effect of Materials on Muscle and Bone[2]

3. Terminology

3.1 *Description of a Term Specific to this Standard:*

3.1.1 *biocompatibility assay*—a comparison of the tissue response produced through the close association of the implanted candidate material to its implant site within the host animal to that tissue response recognized and established as suitable with control materials.

4. Summary of Practice

4.1 Under aseptic conditions, test specimens of the candidate material and of controls are inserted into a muscle or group of muscles of the animal host. After a period of time the animals are euthanized. The tissue reactions to implants of the candidate material during the acute to subchronic time period of healing are compared with tissue reactions to control materials which have a well characterized response. The implants are not subject to major stress while *in situ*.

5. Significance and Use

5.1 The use of *in vivo* implantation techniques for characterizing the biocompatibility of materials to be utilized in various medical applications provides a unique assessment of such materials not achieved by other procedures. Physical characteristics (that is, form, density, hardness, surface finish) can influence the character of the tissue response to the test materials.

5.2 This practice is intended as a rapid screening procedure for determining the acceptability of candidate materials. It would be invoked prior to using the long-term tests described

[1] This practice is under the jurisdiction of ASTM Committee F-4 on Medical and Surgical Materials and Devicesand is the direct responsibility of Subcommittee F04.16 on Biocompatibility.

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

in Practice F 981. It is understood that for some applications additional tests, including long-term implantation studies, may be required to assess the final suitability of the candidate materials.

5.3 This practice may not be appropriate for all types of implant applications. The user is cautioned to consider the appropriateness of the method in view of the materials being tested, their potential applications, and the recommendations contained in Practice F 748.

6. Test Preparation

6.1 Rabbits, rats, or other animals may be used as test hosts. The following procedure is written for New Zealand white rabbits, a commonly used test host but the procedure can be adapted with few alterations to other test hosts.

6.2 *Test Hosts and Sites*:

6.2.1 Choose healthy adult rabbits that weigh more than 2.5 kg and whose paravertebral muscles are sufficiently large to allow for implantation of the test specimens.

6.2.2 The paravertebral muscle shall serve as the test site for implants. (The gluteal muscles of rats have been used as test sites by some investigators.)

6.2.3 *Preparation of Rabbits*—On the day of the implantation or up to 20 h before implantation, clip the fur of the animals on both sides of the spinal column. Remove loose hair.

6.3 *Selection of Control Materials*:

6.3.1 Selection of control material(s) should be based on their prior acceptable use in medical applications similar to those proposed for the candidate test material and is not restricted to those listed in 6.3.2.

6.3.2 Metallic control materials, which have been demonstrated to elicit minimal tissue reactions, are the metal alloys, such as in Specifications F 75, F 90, F 136, F 138, F 562, or F 563, or a ceramic, such as, alumina F 603. A suitable polymeric control material is found in polyethylene Specification F 648.

NOTE 1—There are times when use of a positive control can help to clarify the character of the tissue response to the candidate test sample.

6.3.3 If the most appropriate control material is expected to elicit a tissue response greater than that normally observed with Negative Control Plastic or the alloys cited above, samples of these latter materials may be implanted as controls on the surgical technique.

7. Test Specimens

7.1 *Fabrication*—Each implant shall be fabricated, finished, and its surface cleaned in a manner appropriate for its projected application in humans. Dense metal implants should be finished in accordance with Practice F 86. The size, shape, and surface of test and control implants shall be as similar as is practically possible.

7.2 Implant sizes are left to the discretion of the investigator. Implants in the size range 1 by 10 mm (0.04 by 0.4 in.) to 3.2 by 12 mm (0.125 by 0.5 in.) have often been used. They may be of circular or square cross section. The edges of the specimens should be as smooth as possible to avoid additional mechanical trauma upon implantation.

7.3 *Implantation Period*:

7.3.1 The insertion of all implants into any one animal shall be done at the same surgical session.

7.3.2 Implant evaluation should be performed at 7 and 30 d so that an accurate characterization of both the test and control materials can be made during the acute and subchronic stages of the healing tissue response. Three animals will be used for each sample period, that is, 3 at 7 d, and 3 at 30 d.

NOTE 2—Some investigators have found that extending the test to include a third group of animals maintained for 90 d can provide additional data on the host response to the implant material.[3]

8. Procedure

8.1 *Implantation*:

8.1.1 The recommended method of implantation is by hypodermic needle or tube and trochar. For larger diameter samples, an incision of appropriate size will be required to permit passage of the larger diameter tube. If this technique is not convenient, however, other equivalent implantation techniques judged appropriate may be used. These should be reported as in 9.1. The implantation must be done using aseptic procedures.

8.1.2 *Preparation of Test Specimens*—The specimens should be fabricated as described in 7.1 and prepared for implantation following the procedure in either 8.1.2.1 or 8.1.2.2.

8.1.2.1 Sterilize each specimen as appropriate for final application and, using aseptic technique, insert it into a sterile needle or tube; or,

8.1.2.2 Insert the specimen into a needle or tube, protect the ends with an appropriate cover, and sterilize the assemblies in an appropriate manner.

NOTE 3—Allow for proper degassing if sterilizing agents such as ethylene oxide are used.

NOTE 4—If the materials to be tested are harder than the materials from which the handling instruments are made, there is the danger of surface contamination of the test specimens by wear from the instruments which can disturb the results (for example, ceramic test specimens implanted with metal instruments). If such test specimens must be handled, soft textile or plastic should be used between the implants and the instruments. Of course, care must be taken that none of these auxiliary protecting materials remain in the implantation wound.

8.1.3 The animals should be anesthetized with a commonly used anesthetic agent to a degree deep enough to prevent muscular movement, such as twitching. Properly scrub the clipped skin surface of the animal.

8.1.4 Implant four specimens of the sample into the paravertebral muscle on one side of the spine of each rabbit, about 2.5 cm from the mid-line and parallel to the spinal columns, and about 2.5 cm apart from each other. In a similar fashion, implant four specimens of the control material in the corresponding muscle on the opposite side of the spine of each animal.

8.1.5 In cases where the negative control is other than specified in 6.3.2 and may be expected to elicit more than a

[3] Turner, E., Lawrence, W. H., and Autian, J., "Subacute Toxicity Testing of Biomaterials Using Histopathological Evaluation of Rabbit Muscle Tissue," Journal of Biomedical Materials Research, Vol 7, 1973, pp. 39–58.