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AMERICAN SOCIETY FOR TESTING AND MATERIALS
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Standard Practice for ASSESSMENT OF COMPATIBILITY OF NONPOROUS POLYMERIC MATERIALS FOR SURGICAL IMPLANTS WITH REGARD TO EFFECT OF MATERIALS ON TISSUE[1]

This Standard is issued under the fixed designation F 469; 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.

1. Scope

1.1 This practice covers a series of experimental protocols for biological assays of tissue reaction to nonporous (also nonfibrous) polymeric materials for surgical implants with regard to the effects of the material on animal tissue in which it is implanted. The experimental protocol is not designed to provide a comprehensive assessment of the systemic toxicity, carcinogenicity, teratogenicity, or mutagenicity of the material. It applies only to materials with projected applications in human subjects where the materials will reside in skeletal or soft tissue for time periods in excess of 30 days. Cardiovascular applications and applications in other organ systems or tissues for which these protocols may be inappropriate are excluded. Control materials will consist of any one of the metal alloys in Specifications F 67, F 75, F 90, or F 138.

2. Applicable Documents

2.1 *ASTM Standards:*

F 67 Specification for Unalloyed Titanium for Surgical Implant Applications[2]

F 75 Specification for Cast Cobalt-Chromium-Molybdenum Alloy for Surgical Implant Applications[3]

F 86 Recommended Practice for Surface Preparation and Marking of Metallic Surgical Implants[3]

F 90 Specification for Wrought Cobalt-Chromium-Tungsten-Nickel Alloy for Surgical Implant Applications[3]

F 138 Specification for Stainless Steel Bars and Wire for Surgical Implants (Special Quality)[3]

F 361 Recommended Practice for Experimental Testing of Biological Compatibility of Metals for Surgical Implants[3]

2.2 *Other Document:*

Guide for the Care and Use of Laboratory Animals[4]

3. Summary of Practice

3.1 This practice covers the preparation of implants, the number of implants and test hosts, test sites, exposure schedule, and methods of implant retrieval and tissue examination. A report shall be made of gross and microscopical examination of each test site. Histological criteria for evaluating tissue reaction are provided.

4. Significance

4.1 This is a test protocol for comparing the local tissue response evoked by polymeric materials, from which surgical devices might ultimately be fabricated, with the local tissue response elicited by control materials currently accepted for the fabrication of surgical devices. Currently accepted materials are

[1] This practice is under the jurisdiction of ASTM Committee F-4 on Medical and Surgical Materials and Devices, and is the direct responsibility of Subcommittee F04.20 on Resources.

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[2] *Annual Book of ASTM Standards*, Parts 8 and 46.

[3] *Annual Book of ASTM Standards*, Part 46.

[4] Publication No. (NIH) 74-23, 1923. Available from the Department of Health, Education and Welfare, Washington, D.C.

metals (and metal alloys, see 2.1) that were standardized on the basis of acceptable long-term clinical experience. The metal controls consistently produce cellular reaction and scar to a degree that has been found to be acceptable to the host.

5. Test Hosts and Sites

5.1 Rats (strains in which the incidence of tumors is low), rabbits, and dogs are to be used as test hosts for soft tissue implants, while rabbits and dogs are to be used as test hosts for bone implants.

5.2 Either the paravertebral muscle or femur can serve as the test site for the implants. However, the same site must be used for all the implants in all the animal species.

5.3 Twenty rats, twelve rabbits, and six dogs will be used for studies utilizing intramuscular implants, while twelve rabbits and six dogs will be used for bone implants.

5.4 The schedule for the sacrifice of animals is given in Table 1.

6. Test Specimens

6.1 *Fabrication*—Each implant shall be fabricated and finished, and its surface cleaned in a manner appropriate for its projected application in human subjects.

6.2 *Sizes and Shapes of Implants for Insertion in Muscle:*

6.2.1 For rats, 2-mm diameter by 6-mm long solid cylindrical implants shall be used.

6.2.2 For rabbits, 4-mm diameter by 12-mm long solid cylindrical implants shall be used.

6.2.3 For dogs, 6-mm diameter by 18-mm long solid cylindrical implants shall be used.

6.3 *Sizes and Shapes of Implants for Insertion in Bone:*

6.3.1 For rabbits, 2-mm diameter by 6-mm long solid cylindrical implants shall be used.

6.3.2 For dogs, 4-mm diameter by 12-mm long solid cylindrical implants shall be used.

6.3.3 If the length of the bone implants need be less than that designated because of anatomical constraints, such should be reported in accordance with 11.1.

6.4 *Numbers of Test and Control Implants:*

6.4.1 In each rat, there shall be one control implant and one test implant.

6.4.2 In each rabbit, there shall be two test implants and one control implant in the muscle on each side of the spine or in each femur.

6.4.3 In each dog, there shall be four test implants and two control implants on each side of the spine or in each femur.

7. Conditioning

7.1 Remove all surface contaminants and rinse all test and control implants in distilled water prior to sterilization.

7.2 Package and sterilize all implants in the same way as is used for packaging and sterilizing similar materials for human implantation.

7.3 After final preparation and sterilization, handle the test and control implants with great care to ensure that they are not scratched, damaged, or contaminated in any way prior to insertion.

7.4 Report all details of conditioning in accordance with 11.1.

8. Implantation Period

8.1 The insertion of all the test and control implants into any one animal will be done at the same surgical session. The period of implantation thus coincides with the sacrifice period (see 5.4).

9. Procedure

9.1 *Implantation*—Use surgical methods similar to those described in Recommended Practice F 361, using appropriate drill sizes for the bone implants (see 6.3). Take care to avoid damage to or contamination of the surface of the implants during insertion in the test site. Use standard suture material to close all wounds. The sutures used to close the muscle wounds should be a distance of at least 5 mm from the muscle implants. Report details of surgical procedure in accordance with 11.1.

9.2 *Postoperative Care:*

9.2.1 Care of the animals should be in accordance with accepted standards as outlined in *Guide for the Care and Use of Laboratory Animals*.

9.2.2 Carefully observe each animal during the period of assay and report any abnormal findings.

9.2.3 If infection or injury of the test implant site invalidates the results, replace the