Designation: F1904 – 14

Standard Practice for Testing the Biological Responses to Particles *in vivo*[1]

This standard is issued under the fixed designation F1904; 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 practice covers the production of wear particles and degradation products from implanted materials that may lead to a cascade of biological responses resulting in damage to adjacent and remote tissues. In order to ascertain the role of particles in stimulating such responses, the nature of the responses, and the consequences of the responses, established protocols are needed. This is an emerging, rapidly developing area and the information gained from standard protocols is necessary to interpret responses. Some of the procedures listed here may, on further testing, not prove to be predictive of clinical responses to particulate debris. However, only the use of standard protocols will establish which are useful techniques. Since there are many possible and established ways of determining responses, a single standard protocol is not stated. However, this recommended practice indicates which necessary information should be supplied with test results. For laboratories without established protocols, recommendations are given and indicated with an asterisk (*).

1.2 This standard is not designed to provide a comprehensive assessment of the systemic toxicity, carcinogenicity, teratogenicity, or mutagenicity of the material.

1.3 *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 limitations prior to use.*

2. Referenced Documents

2.1 *ASTM Standards:*[2]

F561 Practice for Retrieval and Analysis of Medical Devices, and Associated Tissues and Fluids

F619 Practice for Extraction of Medical Plastics

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

F1877 Practice for Characterization of Particles

3. Summary of Practice

3.1 Biological responses to particles testing may be done using specimens from animals being tested in accordance with the Practice F748 matrix for irritation and sensitivity, or for implantation. If particles were implanted during the testing procedures or generated during the experimental time period, the response to those particles may form a part of the overall investigation of response to particles. Blood, organs, or tissues from the animals may be used.

3.2 Biological responses to particles may be tested using the actual particulate materials or extracts in accordance with Practice F619. The increased surface area of small particles may enhance the amount of extracted substances but, since the response to particles may be related to the physical size, shape and composition, the use of only extracts will not completely address the question of the impact of particle formation on the tissue response and actual implantation or other testing of particles should be included as a part of the characterization of tissue response when particle generation is likely during actual usage. These materials or extracts may be used in *in vivo* tests or for the *in vitro* tests. Particles generated by other methods may also be used. The method of generation shall be described.

4. Significance and Use

4.1 This practice is to be used to help assess the biocompatibility of materials used in medical devices. It is designed to test the effect of particles from the materials on the host tissues.

4.2 The appropriateness of the methods should be carefully considered by the user since not all materials or applications need to be tested by this practice. The validity of these studies in predicting the human response is not known at this time and studies such as those described here are needed.

4.3 *Abbreviations Used:*

4.3.1 *CD*—Cluster differentiation.

4.3.2 *DNA*—Deoxyribonucleic acid.

4.3.3 *EDS*—Energy dispersive X-ray spectroscopy.

4.3.4 *EU*—Endotoxin unit.

4.3.5 *HLA*—Human leukocyte antigens.

4.3.6 *LAL*—Limulus amebocyte lysate.

[1] This practice is under the jurisdiction of ASTM Committee F04 on Medical and Surgical Materials and Devices and is the direct responsibility of Subcommittee F04.16 on Biocompatibility Test Methods.

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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.