



Standard Guide for Pre-clinical *in vivo* Evaluation in Critical Size Segmental Bone Defects¹

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1. Scope

1.1 This guide covers general guidelines for the *in vivo* assessment of tissue-engineered medical products (TEMPs) intended to repair or regenerate bone. TEMPs included in this guide may be composed of natural or synthetic biomaterials (biocompatible and biodegradable) or composites thereof, and may contain cells or biologically active agents such as growth factors, synthetic peptides, plasmids, or cDNA. The models described in this guide are segmental critical size defects which, by definition, will not fill with viable tissue without treatment. Thus, these models represent a stringent test of a material's ability to induce or augment bone growth.

1.2 Guidelines include a description and rationale of various animal models including rat (murine), rabbit (leporine), dog (canine), goat (caprine), and sheep (ovine). Outcome measures based on radiographic, histologic, and mechanical analyses are described briefly and referenced. The user should refer to specific test methods for additional detail.

1.3 This guide is not intended to include the testing of raw materials, preparation of biomaterials, sterilization, or packaging of the product. ASTM standards for these steps are available in the Referenced Documents (Section 2).

1.4 The use of any of the methods included in this guide may not produce a result that is consistent with clinical performance in one or more specific applications.

1.5 Other pre-clinical methods may also be appropriate and this guide is not meant to exclude such methods. The material must be suitable for its intended purpose. Additional biological testing in this regard would be required.

1.6 The values stated in SI units are to be regarded as standard. No other units of measurement are included in this standard.

1.7 *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

F565 Practice for Care and Handling of Orthopedic Implants and Instruments

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 Bone

F1983 Practice for Assessment of Selected Tissue Effects of Absorbable Biomaterials for Implant Applications

F2150 Guide for Characterization and Testing of Biomaterial Scaffolds Used in Tissue-Engineered Medical Products

2.2 Other Documents:

21 CFR Part 58 Good Laboratory Practice for Nonclinical Laboratory Studies³

21 CFR 610.12 General Biological Products Standards—Sterility³

3. Terminology

3.1 Definitions:

3.1.1 *bone regeneration*—the formation of bone that has histologic, biochemical, and mechanical properties similar to that of native bone.

3.1.2 *bone repair*—the process of healing injured bone through cell proliferation and synthesis of new extracellular matrix.

¹ This guide is under the jurisdiction of ASTM Committee F04 on Medical and Surgical Materials and Devices and is the direct responsibility of Subcommittee F04.44 on Assessment for TEMPs.

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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 Available from U.S. Government Printing Office Superintendent of Documents, 732 N. Capitol St., NW, Mail Stop: SDE, Washington, DC 20401, <http://www.access.gpo.gov>.