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Standard Guide for Biocompatibility Evaluation of Medical Device Packaging Materials[1]

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1. Scope

1.1 This guide provides information to determine the appropriate testing for biocompatibility of materials (or packaging materials) in sterile barrier systems used to contain a medical device.

1.2 *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 to determine the applicability of regulatory limitations prior to use.*

2. Referenced Documents

2.1 *ASTM Standards:*[2]

F17 Terminology Relating to Flexible Barrier Packaging

2.2 *Other Standards:*

ANSI/AAMI/ISO 11607 Packaging for Terminally Sterilized Medical Devices

ISO 10993-1:2009 Biological Evaluation of Medical Devices – Part 1: Evaluation and Testing

USP <1031> The Biocompatibility of Materials Used in Drug Containers, Medical Devices, and Implants

FDA – Center for Devices and Radiological Health: Required Biocompatability Training and Toxicology Profiles for Evaluation of Medical Devices (#G95-1)

3. Terminology

3.1 *Definitions*—For terminology related to barrier materials for medical packaging see Terminology F17.

3.2 *Definitions of Terms Specific to This Standard:*

3.2.1 *biocompatibility*—the inherent ability of a material to remain biologically inert with the host in its intended application.

3.2.2 *biocompatibility testing*—the series of chemical and biological tests that a material is subjected to in order to determine the ability of the material to remain biologically inert with the host in its intended application.

3.2.3 *extent of contact*—the degree to which the packaged device will contact the patient (refer to ISO 10993-1 for levels of contact of the device with the human body). When referring to the packaging, extent of contact refers to the degree to which the packaging will interact with the device. Degree of packaging contact (interaction) is related to the physical-chemical nature of the packaging materials and the device, the intended use of the device (levels of contact with the body), and the extent to which the packaging may negatively impact the contained device.

3.2.4 *sterile barrier system*—minimum package that prevents ingress of microorganisms and allows aseptic presentation of the product at the point of use.

4. Summary of Practice

4.1 Materials used in packaging are to be evaluated per defined guidelines, such as AAMI/ANSI/ISO 11607. Additional biocompatibility testing for packaging materials may be required based on the extent of material contact with the contained medical device, the subsequent degree to which the packaged device (product) will contact the patient, and the intended use of the device. When selecting the appropriate tests for biological evaluation of medical devices, the chemical characteristics of the device materials, as well as the nature, degree, frequency and duration of the device's exposure to the body must be considered. Similar testing may be considered for medical packaging, when there is not a history of safe use of packaging materials for their intended sue or there may be a question as to whether the packaging may negatively impact the contained device. Guidelines for biocompatibility verification of medical device packaging are based on FDA guidance (Memorandum #G-95), ANSI/AAMI/ISO 10993-1 and USP <1031> The Biocompatibility of Materials Used in Drug Containers, Medical Devices, and Implants. While the scope of these standards does not directly apply to medical device packaging, use of them will address the intent of ISO 11607.

The reader is advised to consult these standards in determining which tests apply for a given packaging application. All

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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.

medical device packages are considered to have indirect patient contact, at a minimum. Therefore, the tests selected will not typically require more extensive testing than that required for medical devices intended for indirect patient contact.

However, test selection should also be based on the extent of contact between the package and the device, and the probability that the package may negatively impact the properties of the contained medical device. For example, a device that is a solid structure is less likely to interact with its packaging than a device composed of a semi-solid or liquid material.

5. Significance and Use

5.1 The compatibility of packaging materials with a medical device is a requirement of many regulatory bodies. Since most medical devices are used or implanted in, around or on the human body, these devices must do no harm. Therefore, the packaging materials that come in contact with the medical device must also be evaluated and determined to be safe for use with the human body in that they have no negative impact on the physical, chemical or biological properties of the device. . This evaluation may include both a study of relevant experience with and actual testing of packaging materials. Such an evaluation may result in the conclusion that no testing is needed if the material has a demonstrable history of safe use in the specific role that is the same as that of the package under design.

The medical device manufacturer determines the need for appropriate testing, with consideration of the device/package interactions, if any. The responsibility of the packaging supplier is typically limited to the performance of cytotoxicity testing.

6. Procedure

6.1 *Select the contact level of packaging material based on its known intended usage.* Consult the referenced ISO, FDA and USP guidances for selection of appropriate biocompatibility tests. Because medical device packages are considered to have indirect patient contact, it is unlikely that the tests selected will exceed the requirements for those medical devices intended for indirect patient contact. However, due to the diversity of medical devices and the packaging materials used for them, it is recognized that all tests identified for a certain contact category may not be necessary for any given packaging material while other materials may require additional testing to become approved.

Variations from standard testing plans may be justified to either reduce or expand tests to be done based on 1) known potential contact levels of the device with the patient, 2) the extent of contact between the package and the device, and 3) the relative risk that the package may interact with the product, resulting in a change to the device's physical, chemical, or biological properties.

NOTE 1—For semi-solid and liquid device packaging, specific attention should be paid to the potential for indirect contact components such as inks, varnish and adhesive to volatilize and migrate through the primary barrier into the product.

The history of use of packages and package materials for various medical device applications can also serve as a valuable resource in verifying the biocompatibility of a package system.

6.2 Prepare samples for testing based on testing facilities requirements. Processing steps and labeling of packages can impact the biocompatibility of a package system. Therefore, it is important to test materials that have been manufactured and processed under "nominal conditions" as well as worst case manufacturing conditions, including anticipated sterilization process extremes. If a material is to be printed, insure that test materials are printed and that documentation includes references for inks and label adhesives used. Record the following documentation regarding test materials:

6.2.1 Supplier's name,

6.2.2 Generic material name,

6.2.3 Complete description of material,

6.2.4 Trade name , or number of material, or both,

6.2.5 Lot number of test samples or other traceability number,

6.2.6 Color of material,

6.2.7 Known additives, secondary ingredients list, and so forth,

6.2.8 Secondary processes conducted on materials, such as cleaning, treating, and so forth,

6.2.9 Intended use of material and intended contact level, and

6.2.10 Intended sterilization method and worst case limits.

6.3 *Coordinate testing by testing facility and receive completion report*. Verify the report has been approved/certified by a company representative that all studies comply with Good Laboratory Practices.

7. Keywords

7.1 biocompatibility; cytotoxicity; medical device; medical device packaging; toxicity