A Practical Guide to ISO 10993-14: Materials Characterization

ISO Working Group 14 is developing a separate standard for materials characterization to lessen the potential for adverse biologic effects caused by materials used in medical devices. Note: this is the second part of an ongoing series of articles on ISO 10993. If you haven't already done so, you might like to read the first part, ISO 10993: An Introduction to the Standard.

The biological evaluation of medical devices is currently governed by the set of standards developed by the International Organization for Standardization (ISO) and known as ISO 10993 or, in the United States, by FDA blue book memorandum #G95-1, which is a modification of ISO 10993-1, "Guidance on Selection of Tests." ISO 10993-1 states that "in the selection of materials to be used in device manufacture, the first consideration should be fitness for purpose having regard to the characteristics and properties of the material, which include chemical, toxicological, physical, electrical, morphological, and mechanical properties." Characterization of medical device materials is thus clearly identified as one of the first steps in their overall evaluation. The standard goes on to note that "the following should be considered for their relevance to the overall biological evaluation of the device: a) the material(s) of manufacture; b) intended additives, process contaminants and residues; c) leachable substances; d) degradation products; e) other components and their interactions in the final product; and f) the properties and characteristics of the final product."
Because of the importance of materials characterization to biological evaluation, ISO Working Group 14 is developing a separate standard on the subject, which will cover requirements for providing information about the chemical composition of materials and devices; the potential for release of leachable substances; and the physical, mechanical, morphological, and predictable biological characteristics of devices. This article provides an overview of the significance of materials characterization and the range of applicable test methods.

WHY CHARACTERIZE MATERIALS?

There are two primary reasons to characterize the materials in medical devices undergoing biological evaluation. The first is to establish a baseline fingerprint of the material so that the results of the biological testing can be firmly linked to a specific material formulation. The identifying characteristics of this formulation can, in turn, be used as manufacturing specifications for the device. The second reason is to determine the presence and nature of any extractable chemicals (including process contaminants and residues as well as substances that leach from the material itself) that may find their way from the device into a human subject (Figure 1). A material that is low (or poor) in extractables is unlikely to cause adverse biological effects unless the types of extractables are extremely potent. On the other hand, the biocompatibility of a material high (or rich) in extractables should be considered suspect until it can be shown that the extractables present are not biologically significant.

Figure 1. Polymeric biomaterials are composed of mixtures of chemicals, some of which are bound to the polymer backbone or into the material matrix while others are free to migrate into the surrounding environment. The identities and abundance of these chemicals determine a material's biocompatibility.

The extent to which a material needs to be characterized depends upon the type of material, the end use of the device, and the function of the material within the device. The more critical the role of the device and the more important the properties of its materials are to device performance, the more detailed the characterization program should be.

CHARACTERIZATION METHODS

A variety of techniques are available to fingerprint materials and define their physical properties, to determine the extent to which components can be extracted from them, and to identify the specific chemical compounds extracted. These tests may be carried out directly on material samples or on material extracts prepared under specified conditions.
Infrared (IR) analysis is used extensively to fingerprint materials. In this test, IR energy is passed through a thin film of material and the amount of energy absorbed at various wavelengths is measured. The result is a chart of wavelength versus absorption that is characteristic of the material (Figure 2). By matching the IR spectrum of an unknown material with that of a known material, proof of identity can be established within the limits of the method.

**Figure 2. Infrared analysis provides a rapid, effective means of identifying a polymeric material and of comparing samples to ensure consistency.**

Thermal analyses are also useful for fingerprinting materials. In thermal gravimetric analysis (TGA), a plot of weight change is made as a material is heated at a known rate. In differential thermal analysis (DTA) and differential scanning calorimetry (DSC), an unknown sample and a reference sample are heated with the aid of a programming device and the temperature difference between the two is measured. Testing also can be conducted to determine the unique melting point, degree of crystallinity, and glass transition temperature of a polymer.

The significant physical properties of a material can be identified with various test instruments. For example, stress/strain relationships such as tension, compression, shear, and flexure are determined with a mechanical testing apparatus. Material hardness is determined by means of a durometer that measures the extent to which the material can be compressed. Surface properties, which are especially important for some specific categories of devices, such as those that contact blood, can often be observed directly using light and scanning electron microscopy (SEM).

Some potential extractables from medical device materials are water soluble, while others are soluble only in nonpolar environments. For materials that will contact body tissues, extraction activity in both polar and nonpolar environments is relevant. The *United States Pharmacopoeia* includes physicochemical tests based on water and isopropanol extracts that are particularly useful in defining materials as rich or poor in extractables and in categorizing a specific material's extractables in general terms, such as nonvolatile residue, residue on ignition, buffering capacity, heavy-metals content, ultraviolet absorption, and turbidity.

Gas-liquid and high-performance liquid chromatography (GLC and HPLC, respectively) are powerful analytical tools that can separate and quantitate volatile and semivolatile chemicals. For materials characterization, these techniques can be used with extracts from, or in some cases solutions of, materials. Chromatography can produce qualitative, fingerprintlike information or, with appropriate standards, can be used to identify and quantitate specific chemical components. IR analysis also can be used to fingerprint the chemicals in an extract from a material, and mass spectroscopy methods can provide identification of specific molecular structures. Atomic absorption spectroscopy (AAS) can determine the amount of specific metals present in a material or its extract, while inductively coupled plasma mass spectrometry (ICP-MS) permits simultaneous determination of all the periodic table elements with a lower limit of detectability in the parts-per-billion range.

**CONCLUSION**
Materials characterization forms the basis for understanding the composition of a medical device material and its potential to have an adverse biological effect when the device is put into use. It also serves as a means to ensure standardization of materials from one lot of devices to the next. As the harmonization of ISO 10993 standards and FDA requirements proceeds, the methods described above will be used by the U.S. device industry to a greater and greater extent to aid in the selection of optimal materials and to control the uniformity of medical products.

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Continue to part three of this series, [ISO 10993-5: Cytotoxicity](#).