NIST workshop on needs for reference biomaterials

On November 13, 1998, a workshop was held at the National Institute of Standards and Technology (NIST) to obtain a clearer assessment of the current needs for reference biomaterials (RBMs) with regard to standards, research, and regulatory purposes. In these applications, the RBMs would be used (as are other reference materials) for any of three main purposes: to help develop accurate methods of analysis (reference methods); to calibrate measurement systems; and to assure the long-term adequacy and integrity of measurement quality assurance programs. The workshop established needs and priorities that strongly reflect the current status of materials selection within three biomaterial areas—orthopedic applications, cardiovascular applications, and tissue-engineered medical products. The workshop was an outgrowth of an interagency agreement among NIST, The National Institutes of Health (NIH), and the Food and Drug Administration (FDA) to cooperate in the development of reference materials. NIST, in cooperation with the NIH, the FDA, and others, is facilitating the development of needed RBMs.

Orthopedic reference biomaterials

Two high-priority RBMs, composed of different forms of ultra-high molecular weight polyethylene (UHMWPE), for the orthopedic industry were identified as: (1) reference bar stock, and (2) particulate UHMWPE, with size, shape, and morphology typical of wear debris found around orthopedic implants. UHMWPE is widely used in artificial joints, but demands for longer-use life and higher performance drive the need for improvements in this material. Each of the material forms identified would be useful for helping to achieve these goals. The reference bar material is needed to replenish the supply of reference material that has been made available through the Hospital for Special Surgery under the direction of Dr. Steve Li. This material has been widely used by industry and researchers to provide a common reference for measurement comparisons and is seen as essential for round robin tests anticipated in the future. The reference particulate was identified as needed to provide a reference baseline for research into the biologic effects of particulate wear debris from joint materials. The reference particulate should provide size, size distribution, and morphology like those found around implants that have suffered aseptic loosening.

Cardiovascular reference biomaterials

Representatives of the cardiovascular industry expressed support for the current RBMs development effort being conducted with support from the NIH. In particular, this involves the development of polyetherurethane reference material. It was concluded that the availability of consistent polyurethane from a supplier of reference materials would be preferable to using off-the-shelf Pellathane® (Dow Chemical Company, Midland, Michigan.). However, industry participants emphasized the need to identify more clearly the important properties for each reference biomaterial and to formulate a clear rationale for each additional reference biomaterial that is proposed for development. They also expressed a variety of opinions on the need for additional RBMs for cardiovascular materials, reflecting the diversity of materials under consideration. One issue for industry was concern that the availability of reference biomaterials may result in a mandate by the FDA that new devices must be fabricated out of materials that are identical to RBMs when such RBMs exist. To address this issue it was emphasized that reference materials may be useful in a number of ways, but the primary purpose for their existence is to aid in measurement technology. This is made clear in the introduction of the NIST Standard Reference Materials (SRM) Catalog, which states, "Through the SRM Program, The National Institute of Standards and Technology (NIST) provides SRMs that are certified for their specific chemical or physical properties. SRMs and RMs [see below] are used for three main purposes: 1) to help develop accurate methods of analysis (reference methods); 2) to cali-

Certain commercial materials are identified in this paper in order to summarize adequately the results of the workshop. Such identification is not intended to imply recommendation or endorsement by any of the authors or their organizations, nor is it intended to imply that the materials or equipment identified are necessarily the best available for the purpose.

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brate measurement systems; and 3) to assure the long-term adequacy and integrity of measurement quality assurance programs. NIST SRMs also constitute part of the National Measurement System infrastructure of the United States and, as such, are essential transfer mechanisms for national and international measurement traceability." Hence, RBMs are intended to aid in measurement technology, and the prevailing view at the NIH, FDA, and NIST is that they should be of help to industry by providing reliable references for ascertaining whether or not desirable characteristics exist for materials used in biomedical devices.

Reference biomaterials for tissue engineering

The third section of the workshop centered on the newly emerging arena of tissue-engineered medical products (TEMPs). This field is in an embryonic state relative to purely acellular biomaterials. A discussion of RBMs for TEMPs was included to promote early discussions of the possible needs for RBMs in this rapidly developing field. One conclusion reached was that although the need for RBMs for TEMPs requires further definition, a definite need for reference tissue cell-lines does exist. A potential commercial source for reference cells was identified. However, further basic academic and industrial research is necessary to define reference cells, including the development of stable, nontransformed cell lines. It was agreed that the best approach for further definition of RBM needs for TEMPs would be for them to be identified in the development of consensus standards through the activities of Division IV of the ASTM F04 Committee on Medical Devices and Surgical Materials and Devices.

Workshop principles and summary

The workshop was sponsored by NIST with the cooperation of the NIH, the FDA, and the Society for Biomaterials. About 40 participants registered for the workshop, with 16 from industry. The workshop was motivated by ongoing discussions on RBMs at meetings of the NIH, The American Society for Testing and Materials, and the Society for Biomaterials. Also, recently (1997) an agreement was signed by the NIH, NIST, and the FDA for cooperation on the development of needed RBMs.

The workshop featured speakers from the NIH, FDA, and the Orthopedic, Cardiovascular, and emerging Tissue Engineered Products industries. While the workshop was able to identify a few immediate needs, it clearly demonstrated the importance of a continuing dialog to identify new RBMs, with much of the impetus seen as arising from needs as they appear defined in national/international consensus standards. Because of the need for stable, nonbiased sources for RBMs, it was concluded that NIST should serve as the repository for suitably developed RBMs.

Standard reference materials (SRMs) and reference materials (RMs)

NIST issues two kinds of reference materials (RMs): (1) NIST Standard Reference Materials (NIST SRMs, accompanied by a document stating the intended purpose and application of the SRM, its certified property value(s) with associated uncertainty(ies), and any other technical information deemed necessary for its proper use); and (2) NIST Reference Materials (NIST RMs, issued with a document containing all the technical information necessary for proper use of the material. There are no NIST *certified* values provided in a report of investigation, and authorship of a report's contents may be an organization other than NIST).

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