

cause interference in the assay system in which the reference material is to be used, which may include cell culture or in vivo assays.

The National Institute for Biological Standards and Control (NIBSC) is a center of the Health Protection Agency in the United Kingdom, reporting to the U.K. Department of Health. Its mission is to safeguard and enhance public health through the standardization and control of biological medicines. The provision of these standards is a central feature of the work of NIBSC (1–4).

Candidate Biological Standards and Reference Materials Processed at NIBSC

Most of the materials are single batch products, indeed the specific combination of biological material and formulants may not be encountered exactly again until the reference material is replaced. Typically, a batch comprises a 0.5- to 1-g fill weight of material in some 100 to 20,000 containers, usually heat-sealed, type I neutral glass ampoules, although glass vials may be used for some reference materials. In general, freeze-drying is tailored to yield a residual moisture of less than 1% weight of the dry weight, and dispensing is performed with a coefficient of variation (CV) of 1% or less for formulations with a plasma-like viscosity or 0.25% or less for aqueous-type materials. Table 1 shows some of the biological materials developed at NIBSC and established by WHO ECBS as International Biological Standards and International Reference Materials during the years 2006/2007 (Table 1).

Typical biological standards are shown in Figure 1.

NIBSC holds and distributes over 500 reference items in catalogue and makes over 5000 shipments to laboratories around the world per year. Figure 2A shows the analysis of the preparation of freeze-dried biological reference materials in Centre for Biological Reference Materials (CBRM) during 2008/2009 according to product type, and Figure 2B shows the distribution by area of application.

NIBSC distributes biological standards and reference materials with a “handling” charge to account for the costs of storage and distribution by general mail. For materials, which have to be shipped by other means, for example, infectious materials via special carrier, this is at the cost of the requestor. Current charges and the catalogue of materials available are available from NIBSCs web site (<http://www.nibsc.ac.uk>).

Quality Management System

NIBSC processing facilities operate under a quality management system independently certified to the international standard ISO 9001:2000. This quality system is a visible sign of NIBSCs commitment to quality for the preparation of reference materials, as is the Institute’s independent accreditation to ISO 17025 for its regulatory batch release testing of biological medicines and other related testing activities. Other materials comply with the In Vitro Diagnostic (IVD) Directive and are *Conformité Européenne* (CE) marked in compliance with ISO 13485. Compliance is facilitated by the use of an Institute-wide specific Reference Material Quality System and other ISO 9001 quality systems that control the reference material development from laboratory analytical work through to the process scale filling and distribution.