12 Freeze-Drying of Biological Standards

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INTRODUCTION

Biological Medicines and Biological Standards

Biological medicines due to their inherent complexity and heterogeneity cannot be adequately characterized solely by physical or chemical means. They include bacterial and viral vaccines, blood and serum products, and other immunological, endocrinological, and cell-based medicines. Biologicals play a significant role in medicine and public health also featuring in transplantation and cell therapy programs. In addition, the growth in biotechnology-derived products has introduced the need for new reference standards for those materials that although not batch-released in a formal manner do undergo postmarketing testing and surveillance, and indeed high-quality reference materials may be invaluable in the comparison of biosimilar/biogeneric products that are now coming to the market.

Many national regulatory authorities make special provisions for the control of biological medicines, reflecting their complex nature and production processes. The functional activity of biologicals in most cases cannot be determined in absolute units; it has to be measured against some reference preparation (standard) of the same material. Usually, the standard is a single large batch of well-characterized biological material dispensed into suitable containers with minimal between-container variation, stored under conditions that ensure good stability prior to use. The large majority of biological standards are therefore freeze-dried for long-term stability and ease of distribution.

The definitive reference material for most biological medicines is the appropriate World Health Organization (WHO) International Biological Standard. These International Standards are the primary benchmark for the relevant biological and thus are the biological equivalent of the kilogram or meter. They are established by WHO after extensive international collaborative studies and meet demanding requirements for consistency and stability. International Biological Standards are generally assigned potency values expressed in terms of International Units of biological activity. WHO International Reference Reagents are biological materials usually selected for their qualitative value and have been studied less extensively than International Biological Standards.

The WHO Expert Committee for Biological Standards (ECBS) assesses and if "appropriate" approves proposals for materials to be recognized as WHO International Standards or Reference Reagents. The criteria reflect the suitability for purpose of the material, stability, reproducibility, and, if freeze-dried, the residual moisture (see sect. "Processing of Biological Standards" for details). There is no requirement for sterility but any microbial contamination should not