Validation Practices for Biotechnology Products

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The quality of the papers in this publication reflects not only the obvious efforts of the authors and the technical editor(s), but also the work of these peer reviewers. The ASTM Committee on Publications acknowledges with appreciation their dedication and contribution to time and effort on behalf of ASTM.

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Foreword

This publication, *Validation Practices for Biotechnology Products,* contains papers presented at the symposium of the same name, held in Gaithersburg, Maryland on 24–25 April 1995. The symposium was sponsored by ASTM Committee E-48 on Biotechnology. James K. Shillenn of the Industrial Modernization Center in Montoursville, Pennsylvania presided as symposium chairman and is editor of the resulting publication.

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OVERVIEW

Since 1962, federal drug law has required that firms producing drugs for administration to humans operate under standards called current Good Manufacturing Practice (cGMP). The purpose of the statutory requirement is to assure that all drugs – including drug products (i.e., finished dosage forms) and drug components (i.e., bulk ingredients) – have the identity, strength, quality, and purity that they purport or are represented to possess. In the past, the FDA has attempted to facilitate the implementation of cGMP standards by providing guidelines in several areas of pharmaceutical production. However, once these guidelines are published by the FDA, they are generally interpreted by the pharmaceutical industry as *de facto* regulatory mandates which often discourage the use of alternative or improved procedures for validation of processes and product quality.

Complicating the validation and product quality issue for manufacturers is the trend over the last few years to extend cGMP principles well beyond the preparation of the final dosage form of pharmaceutical products (Secondary Finishing). The principles of cGMP are now being applied to the upstream or Bulk Primary manufacturing steps, especially in biotechnology. Manufacturing firms are also being encouraged to apply cGMP concepts to the maximum extent as far backward in the processing chain as feasible. In other words, a demonstration of a commitment to total quality, not just validation of the purity of the final product. This commitment to total quality is being asked not only of the producers of final biotechnology and biopharmaceutical products but of producers of bulk materials, suppliers of pharmaceutical equipment and materials, and designers and builders of pharmaceutical facilities.

Understanding and responding to quality issues relating to the production of biological and biotechnology products is rapidly becoming a significant obstacle to the competitiveness of companies that are developing these new products. In general, a company must deal with validation and product quality issues that are based upon the expanding cGMP standards without the benefit of a systematic, research-based, proactive approach to quality improvement and validation issues. Another consequence of the complexity of quality and validation issues in the biotechnology product arena is that many small- and medium-sized companies are finding it increasingly difficult to comply with cGMPs and product validation issues. They do not have the resources to support a large staff of engineers and scientists to develop validation protocols and procedures. Additionally, they are not able to support regulatory specialists who can monitor the FDA's response to regulating and enforcing cGMPs.

To be competitive and to effectively respond to Federal regulations including cGMPs in the case of biological products, biotechnology companies will need to collectively develop and subscribe to common test methods, practices, and standards. Most industries in the world use them. Most industries continue to aggressively develop, review, and revise them. Standards not only help manufacturers respond to providing customers with

exactly what they demand but standards also form the basis for any total quality program. Life science companies are making or are about to make the transition from predominately research and discovery companies to product developers and manufacturers. However, with biotechnology companies trying to take products to market as quickly as possible, the development of industry biotechnology standards in the United States has not been a clear priority for the industry. Although some have called for the FDA to develop more guidelines and standards for the biotechnology industry, the FDA, as well as most companies, do not support this approach.

This Special Technical Publication has been published as a result of the Symposium on Validation Practices for Biotechnology Products, held in Gaithersburg, Maryland. This symposium was the outgrowth of work within ASTM Subcommittee E48.06 to identify areas where standards may be needed. The purpose of the symposium was to present current methods and validation practices that are used to comply with the Food and Drug Administration , current Good Manufacturing Practice (cGMP) and innovative approaches and methods for meeting cGMP requirements for biologicals.The collection of papers published in this volume has been grouped into three major categories. These categories are facilities and equipment validation, process validation and planning, and calibration and change control.

Facilities and Equipment Validation

The papers in this section on facilities and equipment validation are written at varying levels of technical depth. One paper provides project managers with information on managing facilities validation while the other papers provide more detailed technical procedures for validating specific items of equipment including standards and practices for computer validation.

Process Validation and Planning

The section on process validation and planning deals with process validation and the management issues that are as significant as the technical issues for a successful validation program for meeting cGMP requirements. One paper in this section makes an important case for incorporating validations practices into the process development and scale-up phases.

Calibration and Change Control

Biotechnology companies that produce biopharmaceuticals must dedicate considerable resources to the validation of a new facility. After this has been accomplished, the accuracy of the instrumentation that is used to control the process must be validated through a calibration program. The third section on calibration and change control covers this topic as well as practices for documenting changes in equipment or process and validation of disinfectants for biotechnology clean rooms and equipment.

As the biotechnology industry grows and matures, it will discover, as other industries have, that standardization of testing procedures and practices is essential to produce high

quality products and lower production costs. The papers in this publication provide the reader with important information for developing and evaluating standards and procedures for cGMP compliance. ASTM and other professional groups and societies whose members are part of the biotechnology industry, must continue to respond to the need for more standards and to publish and develop voluntary standards or risk lower quality, more government regulation, and higher manufacturing costs. The symposium committee gratefully acknowledges the efforts of the authors and ASTM personnel that have made this publication possible.

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