ISPE

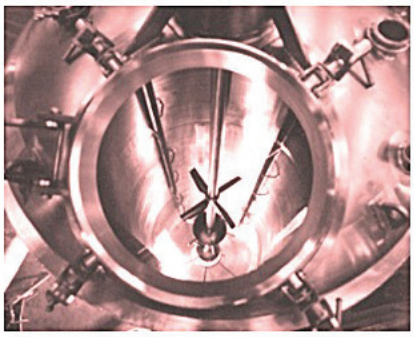
Baseline®
PHARMACEUTICAL ENGINEERING GUIDE
FOR NEW AND RENOVATED FACILITIES

Volume 6

Biopharmaceutical Manufacturing Facilities

Second Edition / November 2013

BioProcess Facilities Designed for Life℠



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This Guide emphasizes the use of closed systems as an approach to mitigating risks associated with the production of biopharmaceuticals. It is meant to assist pharmaceutical manufacturers in the design and construction of new and renovated facilities that are required to comply with the requirements of the US Food and Drug Administration (FDA). The International Society for Pharmaceutical Engineering (ISPE) cannot ensure and does not warrant that a system managed in accordance with this Guide will be acceptable to the FDA or other regulatory authorities. Further, this Guide does not replace the need for hiring professional engineers or technicians.

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Preface

The biopharmaceutical industry has adapted to reflect available technologies, products with more focused patient populations, regulatory conditions, and continued pressures on costs, while maintaining high quality standards. This second edition of the ISPE Baseline® Guide: Biopharmaceutical Manufacturing Facilities develops concepts to reflect how these changes affect biopharmaceutical manufacturing facilities without sacrificing product quality. This Guide discusses the concepts of closed processing and the potential impact of closing a biopharmaceutical drug substance manufacturing process on facility design as an approach to mitigating risks associated with the production of biopharmaceuticals.

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Company affiliations are as of the final draft of the Guide.

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Table of Contents

1 Introduction

1.1 Background

This second edition of the ISPE Baseline® Guide: Biopharmaceutical Manufacturing Facilities intends to further reinforce the concepts described in the first edition of the Guide, provide examples of how these concepts can be put into practice, and detail the value and benefits of the approach described.

The biopharmaceutical industry has adapted to reflect available technologies, products with more focused patient populations, regulatory conditions, and continued pressures on costs, while maintaining high quality standards. This edition of the Guide develops concepts to reflect how these changes affect biopharmaceutical manufacturing facilities without sacrificing product quality, by reducing risk and enhancing the manufacturing control strategy.

As the relevant technology has evolved, the implementation of closed systems has become more accepted and routine; the Guide emphasizes the use of closed systems as an approach to mitigating risks associated with the production of biopharmaceuticals.

1.2 Scope

The ISPE Baseline® Guide: Biopharmaceutical Manufacturing Facilities (Second Edition) applies to new facilities for the development and manufacture of biopharmaceutical drug substances (or Active Pharmaceutical Ingredients (APIs)). This Guide applies to clinical and commercial cGMP production facilities.

Closed systems and closed processing is the central concept throughout this Guide. Closing a bioprocess impacts area classifications, layouts, and how a facility is operated. This Guide is intended to support the development of decisions which allow compliant and cost effective design of biopharmaceutical manufacturing facilities.

Types of drug substances considered in this Guide include:

- Protein therapeutics
- Synthetic proteins
- Polypeptides
- Monoclonal antibodies
- Vaccines[1]
- Biopharmaceutical drug substances isolated from tissues or body fluids
- Transgenic biopharmaceutical drug substances
- Gene therapy biopharmaceutical drug substances
- Stem cells

[1] Note: additional design criteria could be required for specific classes of biopharmaceutical drug substances (e.g., live vaccines). Concepts in this Guide can apply to various scales of operation from single digit liters to tens of thousands of liters.

The facility designs and processes described in this Guide are intended to acknowledge guidelines, such as ICH Guidance for Industry Q7 GMP for APIs [1], PIC/S Guide to GMP for Medicinal Products Part II [2], and ICH Q11 [3], and meet requirements, such as Eudralex Volume 4 GMP Part II Basic Requirements for Active Substances used as Starting Materials [4], and to US GMPs, e.g., 21 CFR Part 211 [5].

The intended audience for this Guide includes:

- Professionals involved in the design, construction, qualification, and operation of biopharmaceutical manufacturing facilities

- Regulatory and quality personnel involved in evaluating technical decisions associated with biopharmaceutical manufacturing facility design

The concepts in this Guide can be applied to other facilities, such as those for blood fractionation, although additional information may be required (e.g., information found in EMA Annex 14 for Blood Fractionation [6] and/or CFDA Annex 4: Blood Products) [7].

Guidance specific to bioprocessing is provided in the ISPE Guide: Biopharmaceutical Process Development and Manufacturing [8]. Further information on related topics discussed in this Guide may be found in other guidance by ISPE, see the ISPE Website for details [9].

This Guide is not intended to be used in the retrofit or evaluation of older facilities; however, the execution of these concepts and strategies can be evaluated and implemented as it benefits production in a major modification to an existing facility.

This Guide is not intended as a replacement for cGMP regulations. This Guide is intended to support options and practices to achieve cGMP compliance.

The processes and facility designs described in this Guide do not apply to filling and/or packaging of sterile drug product.

The appropriate regulatory agencies should be consulted before advancing into detailed design and before starting major construction activities.

1.3 Key Concepts and Terms

Several key concepts and terms are defined in this section of the Guide. Definitions for other terms used in this Guide are provided in the Glossary (see Appendix 3). When these terms are used in the context of this Guide, these definitions should be used.

This Guide discusses the concepts of closed processing and the potential impact of closing a biopharmaceutical drug substance manufacturing process on facility design. Critical Process Parameters (CPPs) and Critical Quality Attributes (CQAs) should be understood before defining process closure and other strategies. Critical process conditions should be understood and facility design should include critical design features.

The following terms used in this Guide are defined as they are used in the following chapters:

Aseptic Operations

Operations that are devoid of measurable (detectable) bioburden. Aseptic operations generally require sterilization of the environment, equipment and process solutions to achieve the sterile state prior to use. Use of Biosafety Cabinets (BSCs) and laminar flow hoods are useful when aseptic open operations are required.