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Points to Consider for
Biotechnology Cleaning
Validation



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Points to Consider for Biotechnology Cleaning Validation Task Force

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1.0 Introduction

Cleaning validation plays an important role in reducing the possibility of product contamination from biopharmaceutical manufacturing equipment. It demonstrates that the cleaning process adequately and consistently removes product residues, process residues and environmental contaminants from the cleaned equipment/system, so that this equipment/system can be safely used for the manufacture of defined subsequent products (which may be the same or a different product). As used in this Technical Report, “product” may be a drug product, bulk active, intermediate, or another type of formulation. If “drug product” is intended, that terminology will be utilized. While cleaning validation for biotechnology manufacturing has many of the same elements as for other pharmaceutical manufacturing, there are enough differences such that a separate Technical Report focusing on biotechnology cleaning validation is appropriate.

Previous PDA documents on cleaning validation, including the 1998 PDA *Technical Report No. 29, Points to Consider for Cleaning Validation* and the 1996 monograph *Cleaning and Cleaning Validation: A Biotechnology Perspective* provide valuable insights for biotechnology manufacturers. (1-2) However, this report presents more updated information that is aligned with life cycle approach to validation and the International Conference on Harmonisation (ICH) guidelines Q8(R2), *Pharmaceutical Development*, Q9, *Quality Risk Management*, and ICH Q10, *Pharmaceutical Quality System*. (3-6) This report also aims to present information in a way that readers can easily utilize to assist in creating a cleaning validation program for their equipment and facilities.

The Biotechnology Cleaning Validation Task Force was composed of European and North American professionals from biotechnology manufacturers, cleaning chemical suppliers, regulatory agencies and consulting companies. This report also underwent a global technical peer review to ensure concepts, terminology, and practices presented are reflective of current science and can be used globally.

Note: For ease of use, this Technical Report includes a list of acronyms used throughout the document. Refer to **Section 16.0**.

1.1 Purpose/Scope

The focus of this Technical Report is on biotechnology manufacturing. Biotechnology manufacturing includes bacterial and cell culture fermentation. While some might exclude plasma fractionation and egg-based vaccine manufacturing from the strict definition of biotechnology, many of the practices and guidance in this report are applicable to plasma fractionation and egg-based vaccine manufacturing. Therefore, examples given will be for biotechnology manufacturing. We have also included a life cycle cleaning validation approach, including design/development of the cleaning process, process qualification (trial protocols runs), and ongoing validation maintenance. These practices and the associated guidance in this Technical Report are based on technical considerations and should be applicable in all regulatory environments.

The intent of this Technical Report is not to provide a detailed plan or detailed road map for a biotechnology manufacturer to perform cleaning validation. Rather, as the title suggests, it presents “points to consider” as one designs a cleaning validation program for biotechnology manufacturing based on an understanding of one’s manufacturing and cleaning processes. In cleaning validation, there are generally *multiple* ways to accomplish the same goal of a compliant, scientifically sound and practical cleaning validation program. Where options are given, the rationales for such options are also generally given. The Biotechnology Cleaning Validation Task Force that developed this document hopes that it will be used in that spirit. Based on an understanding of the unique nature of any individual situation, different approaches or additional issues should also be considered.