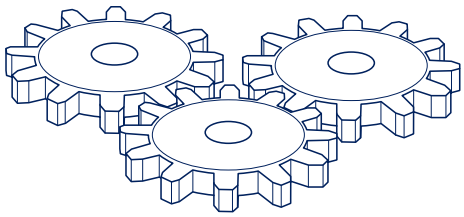
Technical Report No. 29 (Revised 2012)

Points to Consider for Cleaning Validation

PCMO℠
Paradigm Change in Manufacturing Operations℠

2012



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PDA Task Force on Technical Report No. 29 (Revised 2012): Points to Consider for Cleaning Validation

Authors

Destin A. LeBlanc, Cleaning Validation Technologies (Chair)

Gretchen Allison, Pfizer

Jennifer L. Carlson, Genentech

Koshy George, Consultant

Igor Gorsky, ConcordiaValSource

Irwin S. Hirsh, Novo Nordisk AS

Jamie Osborne, Siegfried (USA), Inc.

Greg Randall, Baxter Bioscience

Pierre-Michel Riss, Eli Lilly

George Verghese, STERIS Corporation

Jenn Walsh, Bristol-Myers Squibb

Vivienne Yankah, Sanofi-Pasteur, Ltd.

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Paradigm Change in Manufacturing Operations (PCMO[SM])

PDA launched the project activities related to the PCMO program in December 2008 to help implement the scientific application of the ICH Q8, Q9 and Q10 series. The PDA Board of Directors approved this program in cooperation with the Regulatory Affairs and Quality Advisory Board, and the Biotechnology Advisory Board and Science Advisory Board of PDA.

Although there are a number of acceptable pathways to address this concept, the PCMO program follows and covers the drug product lifecycle, employing the strategic theme of process robustness within the framework of the manufacturing operations. This project focuses on Pharmaceutical Quality Systems as an enabler of Quality Risk Management and Knowledge Management.

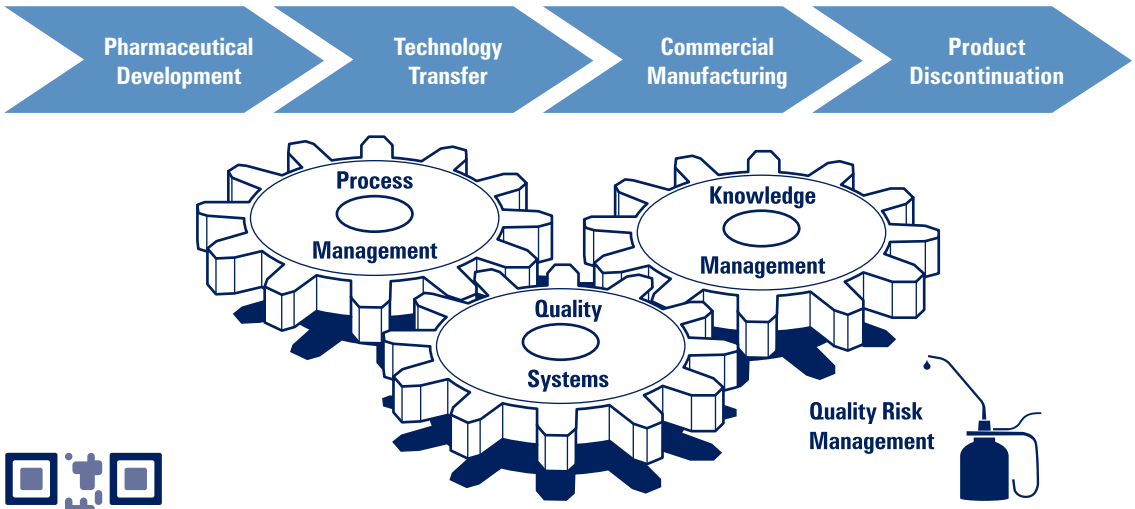
Using the Parenteral Drug Association's (PDA) membership expertise, the goal of the Paradigm Change in Manufacturing Operations Project is to drive the establishment of 'best practice' documents and /or training events in order to assist pharmaceutical manufacturers of Investigational Medicinal Products (IMPs) and commercial products in implementing the ICH guidelines on Pharmaceutical Development (ICH Q8, Q11), Quality Risk Management (ICH Q9) and Pharmaceutical Quality Systems (ICH Q10).

The PCMO program facilitates communication among the experts from industry, university and regulators as well as experts from the respective ICH Expert Working Groups and Implementation Working Group. PCMO task force members also contribute to PDA conferences and workshops on the subject.

PCMO follows the product lifecycle concept and has the following strategic intent:

- Enable an innovative environment for continual improvement of products and systems
- Integrate science and technology into manufacturing practice
- Enhance manufacturing process robustness, risk based decision making and knowledge management
- Foster communication among industry and regulatory authorities

The Product Life Cycle



For more information, including the PCMO Dossier, and to get involved, go to www.pda.org/pcmo

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1.0 Introduction

Cleaning validation plays an important role in reducing the possibility of product contamination from pharmaceutical manufacturing equipment. It demonstrates that the cleaning process adequately and consistently removes product residues, process residues and environmental contaminants from the manufacturing equipment/system, so that this equipment/system can be safely used for the manufacture of specified subsequent products (which may be the same or a different product). As used in this Technical Report, "product" may be a drug product, active pharmaceutical ingredient, intermediate, or another type of formulation. If "drug product" is intended, that terminology will be utilized. Principles and practices given in this report may apply to a variety of manufacturing situations. It is incumbent on the reader to decide the appropriateness of those principles and practices to his/her specific situation.

This report builds on the 1998 *PDA Technical Report No. 29, Points to Consider for Cleaning Validation* ***(1)***. This report also has utilized principles and specific wording from the 2010 *PDA Technical Report No. 49, Points to Consider for Biotechnology Cleaning Validation* ***(2)***. The authors of this revised Technical Report #29 would like to thank the members of the Task Forces who were responsible for those two earlier documents for making our job easier.

This revised Technical Report presents updated information that is aligned with lifecycle approaches to validation and the International Conference on Harmonisation (ICH) guidelines Q8 (R2) - *Pharmaceutical Development,* Q9 - *Quality Risk Management* and Q10 - *Pharmaceutical Quality System* ***(3,4,5)***. Also, this report aims to assist readers who want to create or benchmark a cleaning validation program for their equipment and facilities.

This Task Force was composed of European and North American professionals from pharmaceutical manufacturers, cleaning chemical suppliers, and consulting companies. The report has undergone a global, technical peer review to ensure concepts, terminology, and practices presented are reflective of sound science and can be used globally.

1.1 Purpose/Scope

This Technical Report covers all facets of cleaning validation for pharmaceutical manufacturers, including both manufacturers of APIs and drug products. It also applies to biotechnology manufacturing; however, the reader should consult *PDA Technical Report No. 49, Points to Consider for Biotechnology Cleaning Validation* for more detail and specifics for biotechnology manufacturing ***(2)***. We have included a lifecycle cleaning validation approach, including design/development of the cleaning process, process qualification (including the protocol runs), and ongoing validation maintenance. While the document discusses risk-based approaches, it does not provide details about risk-based manufacturing. PDA has formed a Task Force to write a Technical Report on that topic.

We cannot emphasize enough how important risk analyses are in the selection of and validation of cleaning processes and their validation. This includes the traditional risk analysis based on effects on product quality and on patients. It also includes business risk considerations, such as steps taken to minimize lost product from contamination (even if detection systems are in place to prevent release of that contaminated product for consumer use).

These practices and the associated guidance in this Technical Report are based on technical considerations and should be applicable in all regulatory environments. However, the intent of this Technical Report is not to provide a detailed plan or roadmap for a pharmaceutical manufacturer to perform cleaning validation. Rather, as the title suggests, it presents "points to consider" as one designs a cleaning validation program for process equipment 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. Examples are not meant to be prescriptive or limiting; they merely illustrate a certain practice. Actual acceptable practices should not be considered limited by the discussion in this Technical Report. Based on an understanding of the unique nature of any individual situation, different approaches or additional issues should also be considered. Sound science based on an understanding of the cleaning and manufacturing processes may lead to other equally acceptable practices. The Task Force that developed this document hopes that the report will be used in this spirit and will not be solely used as a checklist.

This report should be considered to be a resource to help guide the development or evaluation of a cleaning validation program. It is not intended to establish mandatory standards for cleaning validation. It is intended to be a single-source overview for pharmaceutical manufacturers that complements existing regulatory guidance and other documents referenced in this document. The reader should also be aware that a specific topic may be discussed in several sections of this Technical Report. Therefore, a more complete perspective may be obtained by considering all relevant sections about a certain topic. Furthermore, while many approaches are presented here, specific approaches utilized for a given cleaning process should be selected based on a good understanding of that process, as well as the appropriateness of the selected practice for that specific situation. It is not enough to merely say that the practice is mentioned as an acceptable one in PDA Technical Report No. 29; each firm should be prepared to defend why the selected approach is a valid one for its operations ***(1)***.

