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Reprocessing of Biopharmaceuticals

PDA Reprocessing of Biopharmaceuticals Technical Report Team

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1.0 Introduction

A validated reprocessing step is a tool pharmaceutical/biopharmaceutical manufacturers can use to bring an active pharmaceutical ingredient (API, aka drug substance) or intermediate that does not meet specification (aka out of specification) into spec or to return a process that has shifted outside its validated operating range to an acceptable state of quality.

The definition of reprocessing for the purpose of this technical report is defined by ICH Q7 ***(1).*** Any strategy for reprocessing must be supported by product and process knowledge. The reason, frequency, and nature of the reprocessing procedure should be carefully evaluated and documented. Costs and risks associated with reprocessing a unit operation must be carefully weighed. Currently, available literature to guide manufacturers in the details associated with implementing a reprocessing procedure is limited.

1.1 Purpose

This technical report presents a reprocessing strategy based on the experiences and practices of a PDA Task Force representing a cross-section of industry professionals. The intent is to provide guidance in the design, development, controls, procedures, validation, regulatory submission, and implementation of reprocessing procedures for recombinant biopharmaceutical manufacturing.

The concepts related to developing a reprocessing strategy are illustrated in two case studies. The first more detailed hypothetical case study involves a chromatography step and provides a data-driven illustration of how the depth and quantity of product/process knowledge influences the reprocessing approach including the regulatory strategy. The second case study is related to refiltration, a more common scenario in manufacturing.

The document is organized to allow the reader to develop a reprocessing strategy for inclusion in their dossier(s) for regulatory approval, standard operating procedures, and validation master plans. The following information represents what the authors consider as a balance of scientific, regulatory, and business considerations in reprocessing.

1.2 Scope

This technical report focuses on recombinant biopharmaceutical products including proteins and polypeptides produced via recombinant and non-recombinant cell-culture expression systems. The guidance is general in nature, and the two case studies illustrate how the general principles may be applied. No attempt is made to encompass all types of unit operations for which reprocessing could be considered.

The reprocessing scenarios considered are generically categorized as reactive and proactive. Although a brief discussion on reactive reprocessing is provided in **Section 3.0,** the primary focus is on proactive reprocessing.

Rework as defined by ICH Q7 (see glossary for definition) is outside the scope of this technical report.

This technical report is not intended to establish mandatory standards but serves as a single-source overview that complements existing guidance documents listed in the reference section. Although the manufacture of APIs intended for use in clinical trials is not specifically addressed, many of the principles may still apply. It is advisable to consult with the appropriate regulatory authority for agreement on the strategies employed for any reprocessing operation.