Technical Report No. 15 Revised 2009 Validation of Tangential Flow Filtration in Biopharmaceutical Applications

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Validation of Tangential Flow Filtration in Biopharmaceutical Applications Task Force

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1.0 Introduction

Technical Report No. 15: Industrial Perspective on Validation of Tangential Flow Filtration in Biopharmaceutical Applications, initially published in 1992, was developed to provide guidance on the validation of tangential flow filtration (TFF) process steps in biopharmaceutical manufacturing. ***(1)*** In the last 15 years, substantial change has occurred in industry—processing equipment has improved, new technology and materials have been introduced, a larger number of products have undergone validation, and, of course, substantial new guidance on validation has been published. ***(2)***

1.1 Purpose

Technical Report No. 15 (Revised 2009): Validation of Tangential Flow Filtration in Biopharmaceutical Applications aims to advance the ideas and information presented in the 1992 original version of TR-15 and bring them up-to-date. Nearly every purification scheme today employs tangential flow filtration and chromatography. The latter subject has also been updated in *PDA Technical Report No. 14 (Revised 2008), Validation of Column-Based Chromatography Processes for the Purification of Proteins*. ***(3)***

The basic tenet of validation has not changed. Its purpose is still to demonstrate with a high degree of confidence that a process performs consistently. However, current practices in tangential flow filter validation now emphasize a continuing cycle of updating process knowledge after the initial validation is complete and stresses a more rigorous scientific approach using risk assessment tools.

This Technical Report will include a detailed discussion of the activities associated with all steps needed to successfully complete validation of tangential flow filtration unit operations for protein purification. Discussions will include tangential flow filtration principles, process development and laboratory studies with scale-down models, manufacturing-scale validation batches, and finally, post-validation tasks, such as process monitoring. This technical report is intended to provide concise guidance and rationale to the scientist or technician with little or no protein purification validation experience; it is not intended to be a step-by-step guide to performing validation.

1.2 Scope

Technical Report No. 15 (Revised 2009), Validation of Tangential Flow Filtration in Biopharmaceutical Applications focuses on validation of tangential flow filtration processes used to manufacture therapeutic proteins and polypeptides produced from recombinant or non-recombinant expression systems that can be characterized with appropriate analytical methods. Some principles may also apply to other product types, such as proteins and polypeptides isolated from tissues and body fluids. However, these products may not be as well characterized as recombinant DNA-derived biopharmaceuticals and monoclonal antibodies. Details surrounding their process validation may differ and are beyond the scope of this document.

This technical report provides a comprehensive overview of strategies that may be used to validate a manufacturing process or unit operation, and it outlines the validation life cycle, including the development and characterization of the tangential flow filtration process, the design of the process equipment, validation of the equipment and process, and post-validation maintenance of the "validated state" through change control, process monitoring and revalidation. The document also contains a concise review of the fundamental principles of tangential flow filtration. A basic understanding of those principles is needed to develop a meaningful validation program.

This technical report does not cover validation as it relates to reprocessing, reworking, aseptic processing of drug products, Process Analytical Technologies (PAT), facilities, design qualification, stability or shipping. References are provided to direct the reader to current sources of information on these topics.

Revised TR–15 is intended to complement *PDA Technical Report No. 42, Process Validation of Protein Manufacturing* by providing more detailed guidance on validation of the tangential flow filtration aspect of the protein purification process. ***(2)*** Similar to TR–42, it does not intend to establish or imply mandatory standards. Use of TFF for virus removal applications is no longer commonly practiced, therefore this is out of scope for this technical report.