Technical Report No. 41
Revised 2008
Virus Filtration

2008

Virus Filtration Task Force

Technical Report Authors

Kurt Brorson, U.S. Food and Drug Administration

Jennifer Campbell, Millipore Corporation

Jeffrey Carter, GE Healthcare

Sherri Dolan, Sartorius Stedim Biotech S.A.

Mani Krishnan, Millipore Corporation

Scott Lute, U.S. Food and Drug Administration

Jerold Martin, Pall Corporation

Mohammed Haque, Pall Corporation

Michael Morgan, Asahi Kasei, Planova Division

Terry Sato, Asahi Kasei, Planova Division

Gail Sofer, SofeWare Associates

Srikanth Sundaram, Generamedix Inc.

Klaus Tarrach, Sartorius Stedim Biotech S.A.

Technical Report Contributors

Amin Abujoub, Biogen Idec Inc.

Hazel Aranha, GAEA Resources Inc.

Damon Asher, Millipore Corporation

Mark Bailey, Eli Lilly and Company

Thierry Burnouf, Human Plasma Product Service

Qi Chen, Genentech, Inc.

Mark Etzel, University of Wisconsin

Chris Dowd, Genentech, Inc.

Charles Felice, Johnson & Johnson

David Jen, Centocor, Inc.

Paul Genest, Millipore Corporation

Uwe E. Jocham, CSL Behring AG

Maik Jornitz, Sartorius Stedim Biotech S.A.

Stanley Kidd, Pall Corporation

Marina Korneyeva, Talecris Biotherapeutics, Inc.

Rich Levy, PDA

Carol Marcus-Sekura, BASI

Ichiro Moroe, Asahi Kasei, Planova Division

Leonard Pease, National Institute of Standards and Technology, U.S. Dept. of Commerce

Mahesh Prashad, Sartorius Stedim Biotech S.A.

Ted Meltzer, Capitola Consultants

Kathryn Remington, Cardinal Health

Cynthia Romero-Arroyo, Ortho Biologics Inc.

Mike Rubino, Eli Lilly and Company

Sakae Satoh, Asahi Kasei, Planova Division (retired)

Michael Shanks, Wellstat Biologics Corp

Ailsa Shepherd, BioReliance Corporation

Thomas Smith, GlaxoSmithKline

Michael Tarlov, National Institute of Standards and Technology, U.S. Dept. of Commerce

William Riordan, University of Wisconsin-Madison

Frank Van Engelenburg, Sanquin Blood Supply Found.

Hannelore Willkommen, Regulatory Affairs & Biological Safety Consulting

Peter Wojciechowski, Johnson and Johnson

Kaoru Yoshinari, Sepa-Sigma, Inc.

The content and views expressed in this technical report are thze result of a consensus achieved by the authoring task force and are not necessarily views of the organizations they represent or the U.S. government.

Virus Filtration

Technical Report No. 41 (Revised 2008)

© 2008 PDA

Table of Contents

Table of Contents

1.0 Introduction

1.1 Purpose/Scope

Biotechnological and biological therapeutic products are often manufactured using materials of animal or human origin, including cultured primary or transformed cells, milk or other components from transgenic animals, natural extracts and human or animal blood plasma. These products are usually proteins that are manufactured by complex manufacturing processes. Although approved recombinant biotherapeutics have an excellent safety record, the risk of contamination by known or unknown pathogens exists, ***(1–6)*** and regulatory agencies worldwide require a demonstration of viral safety prior to clinical use and/or marketing of biopharmaceuticals. ***(3, 7–10)***

The risk of transmission of certain infectious pathogens cannot be completely mitigated by donor screening, vaccination of patients, a single virus inactivation step, or virus testing of cell banks and raw materials. It is desirable to introduce additional robust viral clearance steps in the biotherapeutic purification processes to help reduce or eliminate viruses without compromising the molecular integrity of the products. Virus-removal filters (often incorrectly termed "nanofilters") are specifically designed to remove viruses and other biomolecules from the product (protein) solution through a size-exclusion mechanism.

Virus filtration is performed as part of a manufacturer's overarching virus safety strategy. In this context, virus filtration (size-based removal) is a complement to virus inactivation, both of which contribute to virus clearance. ***(11–21)*** Implementation of virus clearance complements additional measures, such as control over raw materials and testing of cell culture or plasma feedstock. Collectively, these measures form the framework of a virus safety strategy.

This PDA Technical Report addresses virus-removal filters that retain viruses by a size-exclusion mechanism. It explains how they work, recommends how to elect the best filter for various applications, and describes physical and biological/safety characterization of filters test methods, and validation of virus removal. This document should be considered as a guide; it is not intended to establish any mandatory or implied standards.