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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.