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Emerging Methods for Virus Detection

PDA Emerging Methods for Virus Detection Technical Report Team

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1.0 Introduction

The potential for extraneous microbial agents to be present in biological medicines was recognized as early as the late nineteenth century, resulting in enactment of the 1902 Biologics Control Act in the United States. More rigorous federal regulations for the development and testing of biological products were passed following the well-publicized discovery of SV40 in poliovirus vaccines used in the 1950s ***(1,2).***

International and national government organizations and regulatory agencies provide both recommendations and legal requirements, or codes, to manufacturers for developing a suitable testing design to ensure the safety and purity of their products. In the United States, the Food and Drug Administration (FDA) publishes recommendations through Guidance for Industry and Points to Consider documents as well as legal requirements through the Code of Federal Regulations (CFR), which defines and describes testing of biological medicinal products. In the European Union, the European Pharmacopoeia (PhEur) and the European Medicines Agency (EMA), together with the various national governing bodies, publish documents describing required testing practices and expectations. Throughout the rest of the world, attempts have been made to harmonize expectations and testing paradigms, with the goal of assuring that products do not contain infectious adventitious agents. The International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) has made significant progress in establishing worldwide, harmonized best practices for approaches to adventitious agent detection and risk mitigation ***(3,4).*** Additionally, the World Health Organization (WHO) has updated TRS 878, Annex 3, *Recommendations for the Evaluation of Animal Cell Cultures as Substrates for the Manufacture of Biological Medicinal Products and for the Characterization of Cell Banks* ***(5).***

Despite the required virus testing of biologic drugs, rare cases of introduction of adventitious agents into a production stream or product have been reported (**Table 1.0-1**). Of note, the majority of these contamination events were traced to raw materials used during manufacturing. Such events have served to refocus the effort to establish more effective surveillance programs, mitigation strategies, and use methods for enhancing adventitious agent detection. Although current methods for detecting adventitious viruses have provided a generally good safety record of biological medicines over the years, these methods may not detect latent or occult viruses, novel viruses, and even some known viruses. Emerging nucleic based methods have demonstrated potential to fill these gaps for virus detection.