A Simple Solution for Medical Device Viral Ingress Testing of Human Immuno Virus and Hepatitis B Virus

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Abstract

FX174 (Phi X 174) can be used as a model for HIV, HBV, and HCV viral penetration or ingress studies. It is utilized for the following reasons, the significant risk associated with laboratory testing conducted with human pathogens that may compromise safety necessitates that studies be undertaken with non-virulent species such as bacteriophages. Bacteriophage has been utilized as surrogates of mammalian virus in both medical and virology applications. In industry Phi X174 is commonly utilized as a viral surrogate, selection of bacteriophage for model is based on size, morphology, environmental stability, and also non-human infectivity, and rapid assay. Phi X174 closely models blood-borne pathogens like Hepatitis (HCV and HBV) and Human Immunodeficiency Virus (HIV) and is employed in barrier penetration studies. It is an ideal blood borne pathogen model because it has no envelope (like HIV), is 27 nm in size (like HCV) and has a nearly spherical geometry (icosahedral), which is similar to all three pathogens (HIV, HBV, and HCV). It can also be cultivated at high titers similar to HBV and has excellent environmental stability similar to HBV.

Background

510(k) submission to the FDA may include validated barrier efficacy or/and cleaning and disinfection procedures effective against HIV, Hepatitis C, and Hepatitis B virus (HBV) for certain medical devices such as Blood Glucose Meters (BGM) or Infusion Pumps.

The HBV blood concentration in chronically infected asymptomatic persons can up to 10^7 per mL.

Detection of HBV is performed by immunosassay or molecular genetics (i.e. surface antigen (HBsAg) or PCR (HBV NAT). Detection is semi-quantitative through concentration standards and transformation of data to derived viral particle quantity.

HBsAg detection limit is 0.1 ng HBsAg/ml of serum (2 x 10^7 particles/mL serum) and equivalent to 2000 HBV/mL or approximately 5 logs of sensitivity from a known HBsAg detection limit is 0.1 ng HBsAg/ml of serum (2 x10^7 particles/mL serum) and equivalent to 2000 HBV/mL or approximately 5 logs of sensitivity from a chronic asymptomatic state, (Deguchi 2004).

HBV NAT sensitivity is higher but downsides include labor intensive, low throughput, and costly.

Infectivity studies undertaken with mammalian viruses possess limitations such as maintenance of cell lines and require a time consuming monitoring of cytopathic effect such as the formation of plaques, foci of infection, or induction of abnormal cellular morphology, and additionally may require lag times on the order of weeks for cell culture. (Brando 1995).

Surrogate species provide an alternative model system for assay.

510(k) Submissions

Phi X174 has been used as part of validation process of a 510(k) for:
1. Navigator Delivery System, Carticept Medical Inc., K101194
2. Genie, ICU Medical, K070633

Advantages

Key advantages are ease of assay, high titers, and sensitivity of detection (>8 logs). Laboratory testing conducted with human pathogens presents a significant risk that may compromise the safety of the laboratory staff. For these reasons it is justifiable to propose non–virulent bacteriophages to model under appropriate conditions.

Follow Up

1. Identify relevant bacteriophage and construct library
2. Develop protocols for barrier/penetration, cleaning and disinfection studies
3. Feedback from relevant institutions/agency partners
4. Validate methods with industry/agency partners
5. Publish findings towards creation of industrial standards

Examples of Industry Guidance Documents

- EPA, Manual of Methods for Virology. Chapter 16
- FDA, Testing Guidance for Male Condoms Made from New Material (Non-Latex)
- FDA, Guidance for Manufacturers Seeking Marketing Clearance of Ear, Nose, and Throat Endoscope Sheaths Used as Protective Barriers