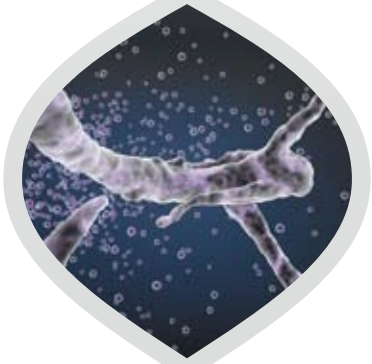
Development Center for Biotechnology

ANIMAL TECHNOLOGY INSTITUTE TAIWAN

Testing Facility for Biological Safety (TFBS)



Process Validation Studies of Viral Clearance

Manufacturers of biopharmaceutical products, such as blood products, monoclonal antibodies, recombinant proteins, and some medical devices derived from animal or human tissues are required to demonstrate the ability to eliminate or inactivate the potential contaminants of the product. A major concern of contamination for biopharmaceutical products during its production is viral contamination. Viral contamination often arises from the source of the cell lines and/or from the use of animal derived raw materials. The ICH Q5A regulatory guideline indicates that a manufacturer of biopharmaceutical products for human use should demonstrate the capability of the manufacturing process to effectively remove or inactivate potential known contaminants. One aspect of assessing the viral safety of biopharmaceutical products is to perform a viral clearance validation study.

Viral Clearance

Viral clearance studies are performed to assess the capability of the purification process to remove and/or inactivate potential viral contaminates likely to be present in or introduced during the production of biopharmaceutical products. Regulatory requirement of viral clearance study varies between countries and regions. In general, a duplicate study of 2 virus, including a robust virus, is required to demonstrate the capability of virus removal / inactivation.

The selection of model and specific virus is depending on 3 major aspects, the source of the study material, the virus detection result of the study material and the characteristic of virus. The virus is spiking into the down-scaled version of purification steps with a known virus titer. By determining the log reduction factor of the virus titer, the ability of a purification step to inactivate or remove virus can be then quantified.

Infectivity assay is the most common and preferred approach to determine the effectiveness of a process step in removing and/or inactivating viral contaminates. Incorporating with real time quantitative PCR into a viral clearance study allows the viral genomic copy number to be determined thereby distinguishing between virus removal and inactivation.

We take a customized approach, including advice and regulatory support in the selection of steps and model virus, scaling down of purification processes and subsequent design of the study protocols, to ensure a successful program is established and performed to meet clients' timelines.

Quality Service and Technical Support

1) Regulatory advisor and senior consultant.
2) Designated project manager as single contact window.
3) GLP compliance.

Facility

1) Newly established facilities with the latest and most advanced equipments on two sites allow us to commence studies with minimal delay.
2) Biosafety level II and level II plus facilities.
3) Independent cell culture and virus production rooms with controlled air flow to avoid cross contamination.
4) Approximately 17 different model viruses available for selection.
5) Optimized high titer viruses.

Example of Processes

Virus Inactivation		Virus Removal	
Chemical	Physical	Chromatography	Nanofiltration
> Organic Solvent	> Dry Heat	> Affinity	
> Detergent	> Pasteurization	> Ion Exchange	
> Caprylate	> Vapor Heating	> Hydrophobic	
> Chaotropes	> High Temperature Short Time	> Gel Filtration	
> Low pH	> Photo Inactivation		
> High pH	> UV with Photoactive Compounds		
> Enzymes	> Gamma Irradiation		
	> Microwave		

Model Virus Panel

Model	Family (-viridae)	Type		Size (nm)	Resistance
BVDV	Flavi	RNA	Enveloped	50-70	Low
HIV	Retro	RNA	Enveloped	80-110	Low
PERV	Retro	RNA	Enveloped	80-110	Low
MuLV	Retro	RNA	Enveloped	80-110	Low
TGEV	Corona	RNA	Enveloped	100-120	Low
bPIV3	Paramyxo	RNA	Enveloped	100-200	Low
HAV	Picorna	RNA	Non-Enveloped	25-30	Med
EMCV	Picorna	RNA	Non-Enveloped	25-30	Med
Reo 3	Reo	RNA	Non-Enveloped	60-80	Med
PReo	Reo	RNA	Non-Enveloped	60-80	Med
PAdV	Adeno	DNA	Non-Enveloped	60-90	Med
HAdV5	Adeno	DNA	Non-Enveloped	60-90	Med
HSV1	Herpes	DNA	Enveloped	120-200	Med
PRV	Herpes	DNA	Enveloped	120-200	Med
PPV	Parvo	DNA	Non-Enveloped	18-24	High
MMV	Parvo	DNA	Non-Enveloped	18-24	High
SV40	Papova	DNA	Non-Enveloped	40-50	High

Contact Us

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