Orthogonal Virus Clearance Technology Platform

- **Low pH Virus Inactivation**
- **AEX virus adsorbtion**
- **Virus removal**
- **UV virus inactivation**

“It is mandatory to demonstrate, that steps in the manufacturing process are capable of inactivating or removing potential viral contaminants.” (Dr. Horst Ruppach, Charles River Laboratories)

This case study refers to a presentation of Dr. Horst Ruppach, Manager Viral Clearance at Charles River Laboratories held on the Upstream and Downstream Technology Forum, September 8-10 2014 at Sartorius Stedim in Göttingen dealing with “Best practices in viral clearance study design execution and reporting to meet current regulatory requirements for recombinant proteins and antibodies”.

Dr. Ruppach talks about the prepositions to run virus clearance studies for clinical phases and marketing authorization under consideration of regulations and guidelines concerned, e.g.:

- EMEA/CHMP/BWP/398498, 2009: Guideline on virus safety evaluation of biotechnological investigational medicinal products,
- FDA (CBER), 1997 Points to consider in the manufacturing and testing of monoclonal antibody products for human use and others.
- ICH Harmonized Tripartite Guideline Q5A (R1) 1999: Viral safety evaluation of biotechnology products derived from cell lines of human or animal origin
- WHO Technical Report, Series No. 924, 2004, Annex 4; Guidelines on viral inactivation and removal procedures intended to assure the viral safety of human blood plasma products chapter 4.2.1, page 184.

He explains orthogonal principles of reduction gives the following recommendations and explanations based on his long term experience as Manager Viral Clearance at Charles River.

He stated:
Virus safety through viral reduction in a manufacturing process is better demonstrated by a documented three-step approach and high reduction factors, rather than a two-step approach and extremely high reduction factors. Extremely high loads, apart from their relevance, and extremely high reduction factors may increase the overall reduction but do not provide significantly higher virus safety.

The definition of effectiveness requires the consideration of many parameters such as: appropriateness of test virus used, design of clearance studies (orthogonal principles of reduction), possible selectivity of inactivation/removal procedures for certain classes of viruses etc.

Sartorius offers a unique technology platform to help you fullfil increasing regulatory requirements in every application. We provide four orthogonal technologies for inactivation and removal of virus particles. You will benefit from the flexibility to choose the right method for your virus clearance process.

Learn more how UVivatec® virus inactivation, Sartobind® membrane chromatography and Virosart® filtration represent today's spearheading technology for quantitative virus clearance. Extend your choice with the FlexAct® VI system for low pH virus inactivation or the FlexAct® VR for virus filtration.

Facts about Charles River Laboratories:

Charles River provides essential products and services to help pharmaceutical and biotechnology companies, government agencies and leading academic institutions around the globe accelerate their research and drug development efforts. Our dedicated employees are focused on providing clients with exactly what they need to improve and expedite the discovery, early-stage development and safe manufacture of new therapies for the patients who need them. To learn more about our unique portfolio and breadth of services, visit www.criver.com.

For more detailed information please look at:

1. Horst Ruppach, Log10 reduction factors in viral clearance studies, Bioprocessing Journal, January 8, 2014

2. Horst Ruppach, Best practices in viral clearance study design execution and reporting to meet current regulatory requirements for recombinant proteins and antibodies, Charles River Laboratories, European Upstream and Downstream Technology Forum, September 8-10 2014, Sartorius Stedim