A Frost & Sullivan White Paper

3M™ Polisher ST Virus Clearance Conquers mAb Solutions

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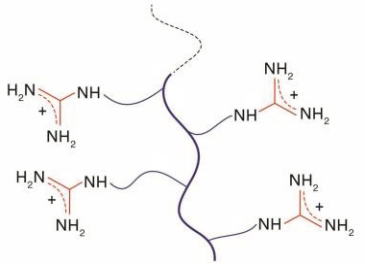
Regulatory authorities require biopharmaceutical companies to demonstrate robust viral clearance by at least two orthogonal process steps. The AEX step is often part of the viral clearance strategy in mAb processes. Being able to demonstrate robust viral clearance under a wide range of process conditions provides flexibility for process development and avoids unwelcome surprises during validation.

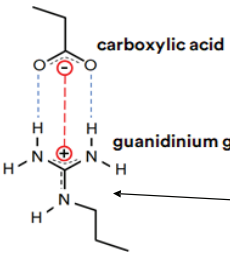
Adsorptive depth filters have been shown to provide viral clearance capability by either electrostatic adsorption or a combination of adsorption and mechanical entrapment. However, implementation of adsorptive filters for claimable impurity and virus clearance in GMP manufacturing processes has been hindered by: 1) relatively poor and variable binding capacity (no consistency), 2) lack of testing methods to demonstrate the post-usage filter integrity, and 3) poor understanding of viral clearance mechanism.

3M™ Polisher ST is designed to operate in pre- or post-use integrity test conditions, accommodates a wide range of operating conditions and has demonstrated the highest impurity removal rates.

Figure 1: Enabling Robust Viral Clearance Using New AEX Ligand Chemistry

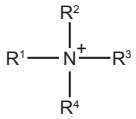
- Guanidinium functional group
- Novel 3M bio-inspired functional ligand design
- Large resonance structure stabilizes positive charge
- Multiple electrostatic-like interactions





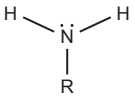
Capable of salt-bridging and hydrogen bonding

Current AEX Ligand Chemistries



Quaternary ammonium (Q)

- Conductivity sensitive



Primary amine (PA)

- Better salt tolerance
- Polyvalent buffer intolerant

Numerous experiments conducted strongly suggest that the HCP and DNA removal is governed predominantly by electrostatic interactions, but additional interactions such as hydrogen bonding also play an important role. They have also demonstrated that the 3M™ Polisher ST technology has a higher HCP removal capacity resulting from salt tolerance.

Current regulations require that the manufacturing process demonstrate the ability to clear model viruses to ensure the safety of these cell-line derived products prior to approval, with additional built-in safety for robustness. In the past, it has been demonstrated that greater than 3–4 log reduction of viruses can be achieved by using ADF post Protein A. 3M™ Polisher ST technology has demonstrated even higher clearance of viruses by filtration post low pH viral inactivation and neutralization.

In order to demonstrate the viral clearance, 3M™ Polisher ST technology was analyzed for clearance of murine viruses at low and high conductivities. Multiple studies have now demonstrated that 3M™ Polisher ST technology is at least as efficient at virus removal as equivalent columns, and due to the unique benefits of guanidium ligand mentioned above often exceed columns in terms of virus clearance.

XMuLV, Reo-3 and PrV all showed > 6 LRV clearance (detection limit) from pH 5 - 7.5, conductivities 3 - 20 mS/cm and in both monovalent (Acetate/Tris) and polyvalent (Citrate/Phosphate) buffers. MVM showed > 4 LRV clearance from pH 5.5 - 7.5, conductivities 5 - 20 mS/cm and in both monovalent (Acetate/Tris) and polyvalent (Citrate/Phosphate) buffers.

3M™ Polisher ST technology has also been tested for viral clearance in actual mAb solutions. Six models covering a wide range of relevant conditions in DSP processes for mAbs were generated to represent real-life processes.

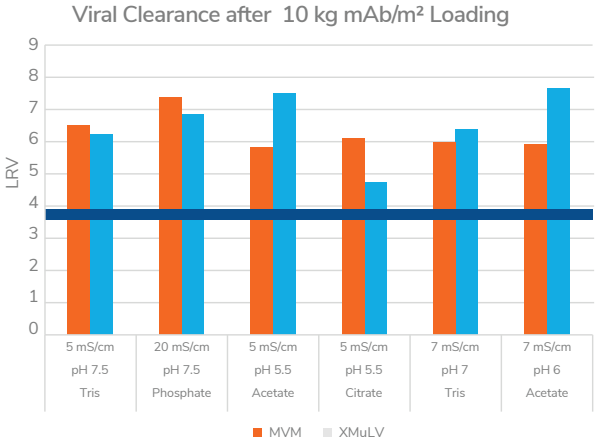
Figure 2: Robust viral clearance in mAb solutions

Viral Clearance studies were performed with MVM and XMuLV using mAb solutions representing legacy, modern and next-gen mAb feed streams.

The Tris pH 7.5 – 5 mS/cm MVM study was performed at Charles River. All other studies were performed at Texcell.

Feed Stream	Buffer	pH	Cond. (mS/cm)	Turbidity	Target HCP (ppm)	Target DNA (ppb)
Legacy	Tris	7.5	5	no	200	20
Legacy	Phosphate	7.5	20	no	200	20
Modern	Acetate	5.5	5	yes	500	1000
Modern	Citrate	5.5	5	no	500	50
NextGen	Tris	7.0	7	no	500	50
NextGen	Acetate	6.0	7	no	500	50

>4 LRV viral clearance was shown for all mAb feed streams



Robust viral clearance of 4 logs or more was shown for all conditions, including low pH, high conductivity or presence of turbidity. Interestingly, robust viral clearance was also observed in citrate buffer. Host cell protein removal typically is much lower in citrate, but process development scientists can still reliably use the product for viral clearance under these conditions.

Virus clearance studies are a core component of the multipronged approach needed to ensure the safety of biologic products. 3M™ Polisher ST technology has been tested for a wide range of conditions with mAb solutions that are representative of real-life DSP processes. Robust viral clearance was shown for conditions including low pH, high conductivity, polyvalent buffers and the presence of turbidity. This level of confidence enables implementation as a true platform tool across different processes in development.

NEXT STEPS

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