

3M Science.
Applied to Life.™

Separation and Purification Sciences Division

3M™ Polisher ST

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September 20th, 2020

Agenda

- 3M overview 公司简介
- Challenges in Biopharmaceutical DSP processes 生物制药下游工艺难点和挑战
- 3M™ Polisher ST 3M™抗高盐层析膜介绍
- Impurity reduction and viral clearance 杂质去除和除病毒应用
- Case study 成功案例
- Summary

3M简介

- Founded in **1902**
- Headquarters: St. Paul, Minnesota, USA
- 2019 Global Sales: **\$32.1 Billion** (~60% International)
- **91,000** 3Mers globally
- ~ **8,000** employees in GCA
- More than **4,500** employees have Ph.D degrees (most of them in chemical engineering)
- **113,000** patents
- One of **30** companies on the Dow Jones Industrial Index

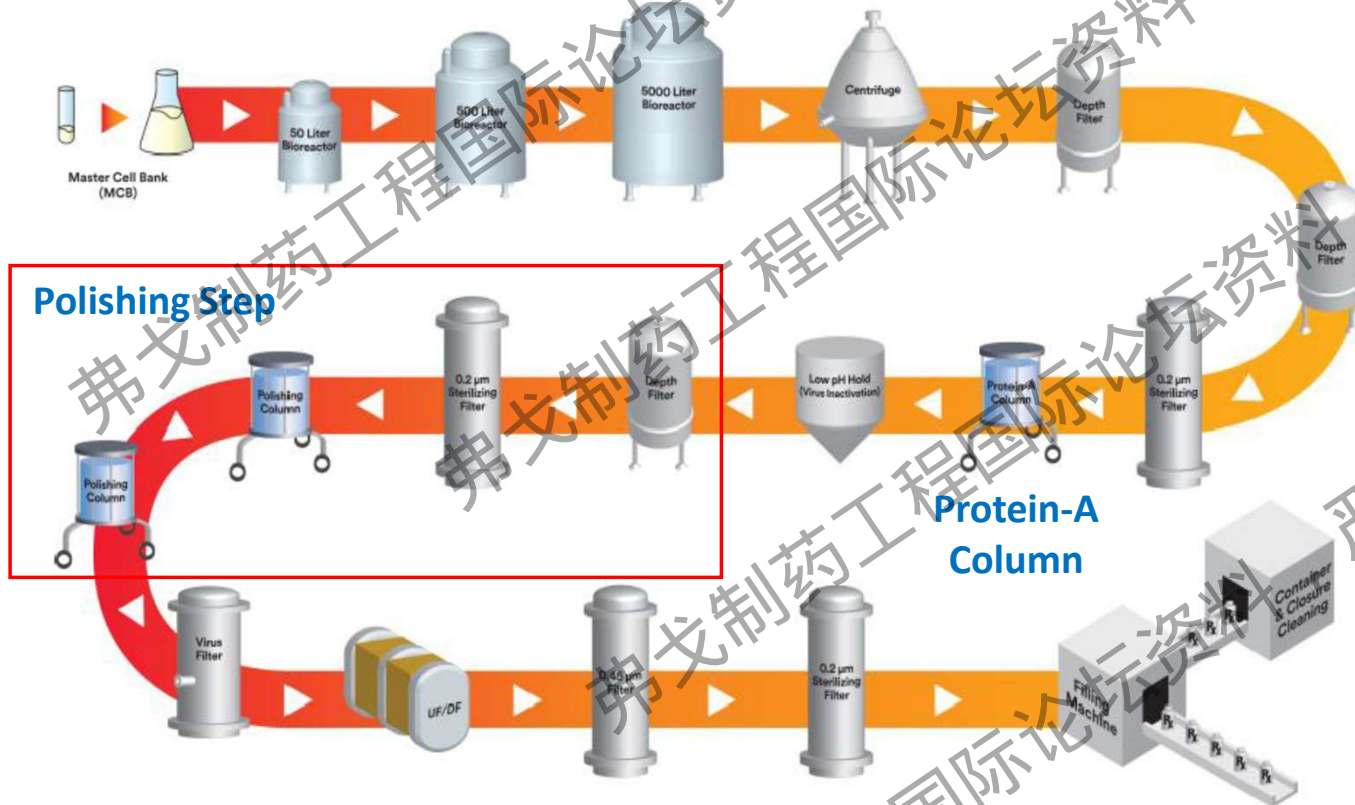


Separation and Purification Science Division

- Prior to 2005, 3M had a small filtration business with bag filters and HEPA grade air filters (Filtrete™)
- A 3M fully owned subsidiary – Dyneon, also offered IEX resins under the trade name Emphaze™, an extraction product Empore™ (later sold to Chinese company) and was in development of a Protein-A resin, and later on, a Protein-A membrane chromatography
- In 2005, 3M acquired CUNO for \$1.35 billion
- CUNO was a liquid filtration company specialized in depth filtration and sterilizing grade membrane filters
- In 2015, 3M acquired Membrana for \$1.0 billion, maker of Liquid-Cell and PES membranes



Platform mAb Production Process



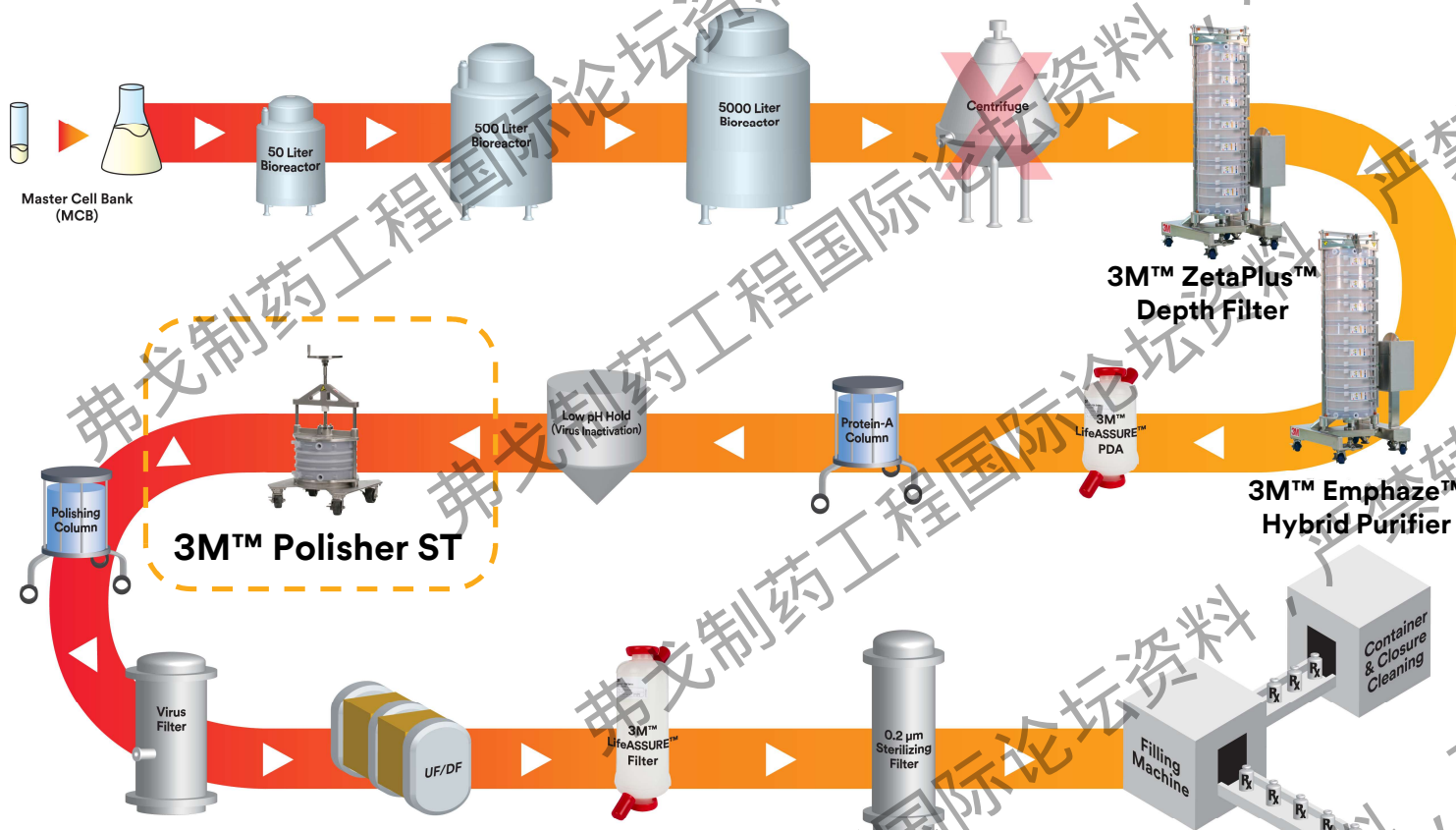
> 10 step process:

- Robust design to ensure the complete removal of a variety of impurities:

- Cells + cell debris
- HCP
- DNA
- Virus
- Bio-burden

- Process variations (especially at the cell culture step) make platformability difficult

Introduction of single use AEX step

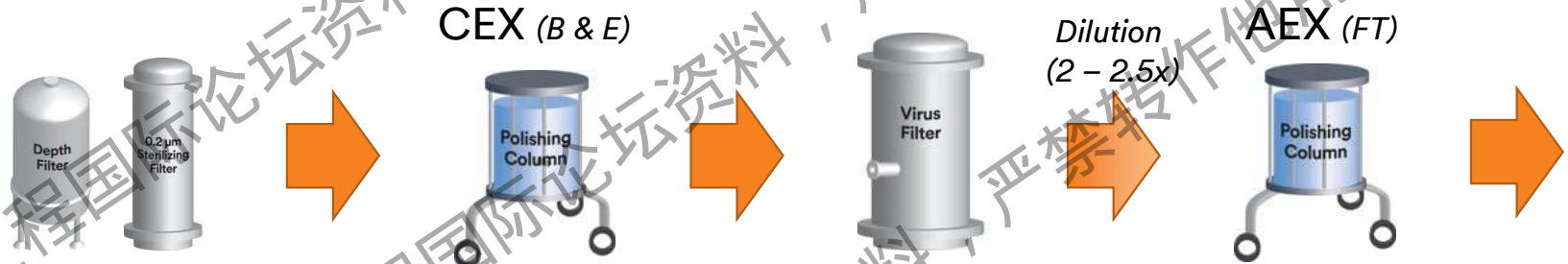


3M technologies provide:

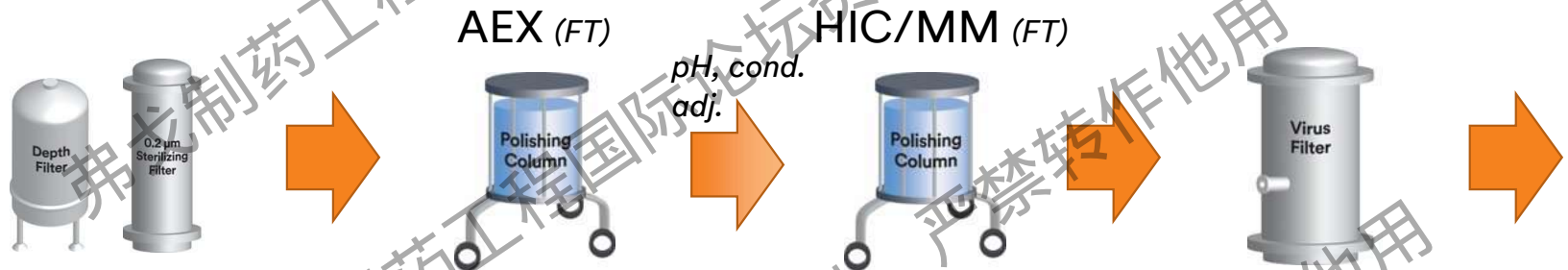
- Higher purity early on
- Process simplification
- Efficiency and reduced total cost of ownership
- Single-use technologies
- Robust, reliable solutions

Polishing Trains in mAb Production

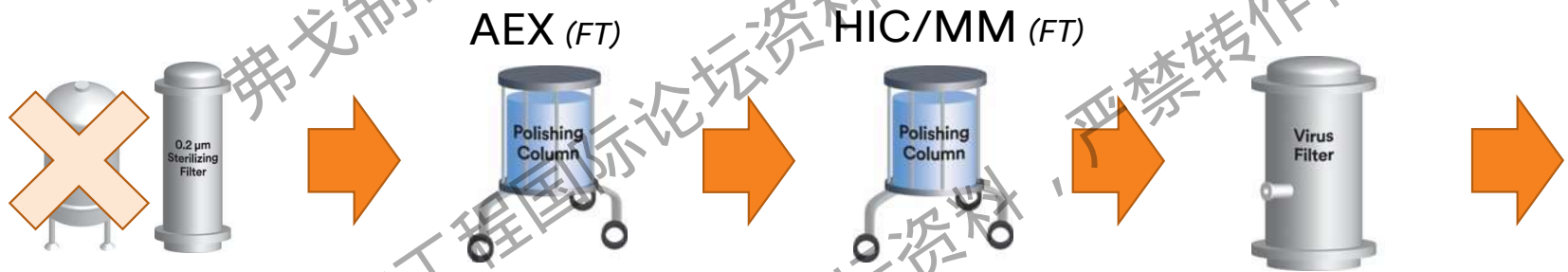
Legacy



Modern



Next gen



3M™ Polisher ST

Advanced single use AEX solution designed to replace reusable AEX polishing column

Reusable AEX Column



3M™ Polisher ST

BC16000



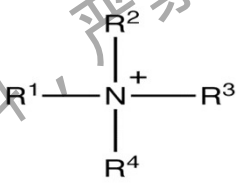
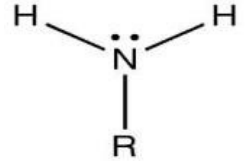
3M™ Polisher ST has:

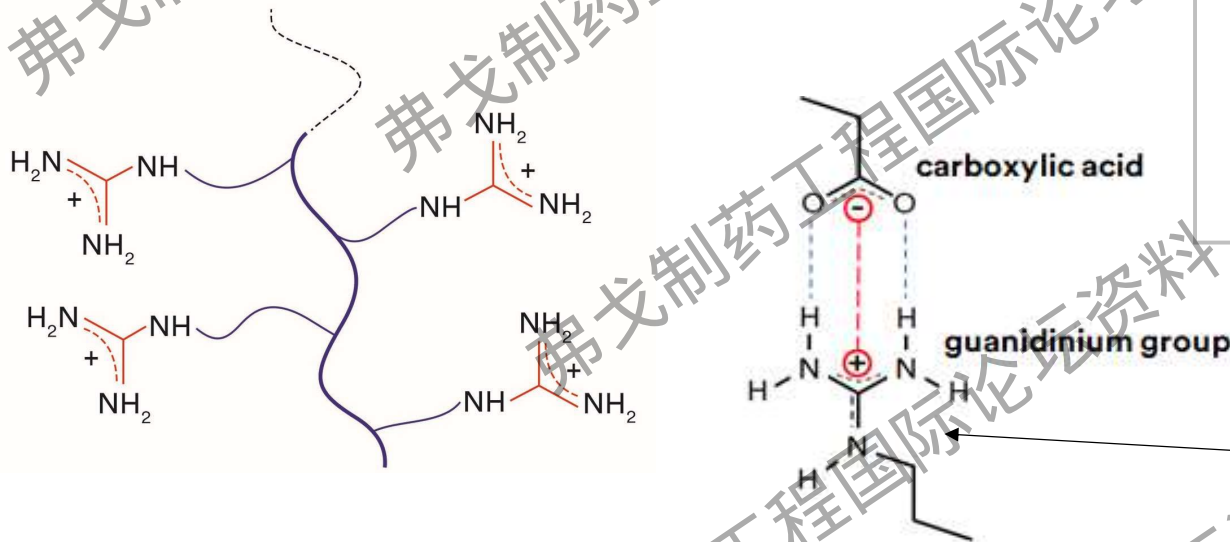
- > 100x mAb loading of typical Q resin (10+ kg/m² target loading)
- Scalability from lab to manufacturing scale
- High salt and low pH tolerance
- Robust viral clearance across very wide range of conditions
- Viral nano-filter protection

3M™ Polisher ST

Enabling robust performance 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

Current AEX Ligand Chemistries	
	
Quaternary ammonium (Q) <ul style="list-style-type: none">• Conductivity sensitive	Primary amine (PA) <ul style="list-style-type: none">• Better salt tolerance• Polyvalent buffer intolerant



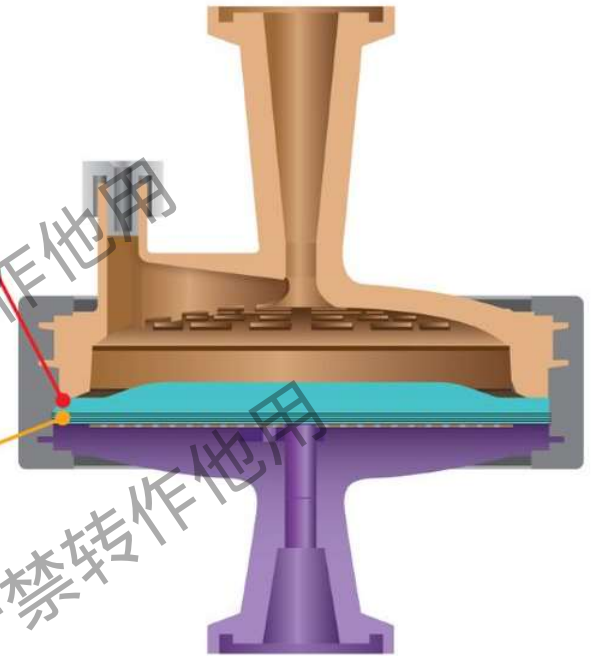
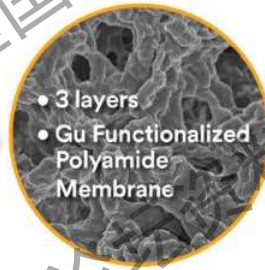
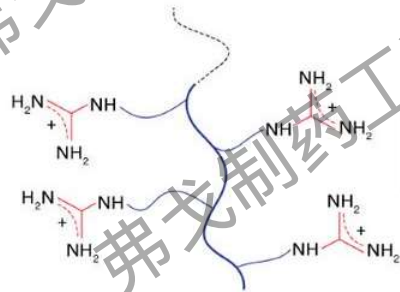
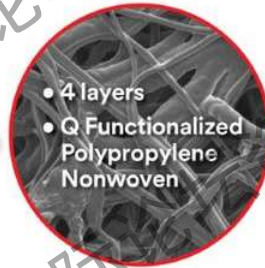
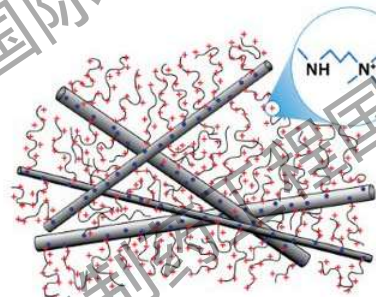
Capable of salt-bridging and hydrogen bonding

3M™ Polisher ST

Capsule construction

- Turbidity reduction (membrane protection)
- DNA capture even at high conductivity (protecting the membrane capacity)

- Host Cell Protein (HCP) capture
- Virus capture



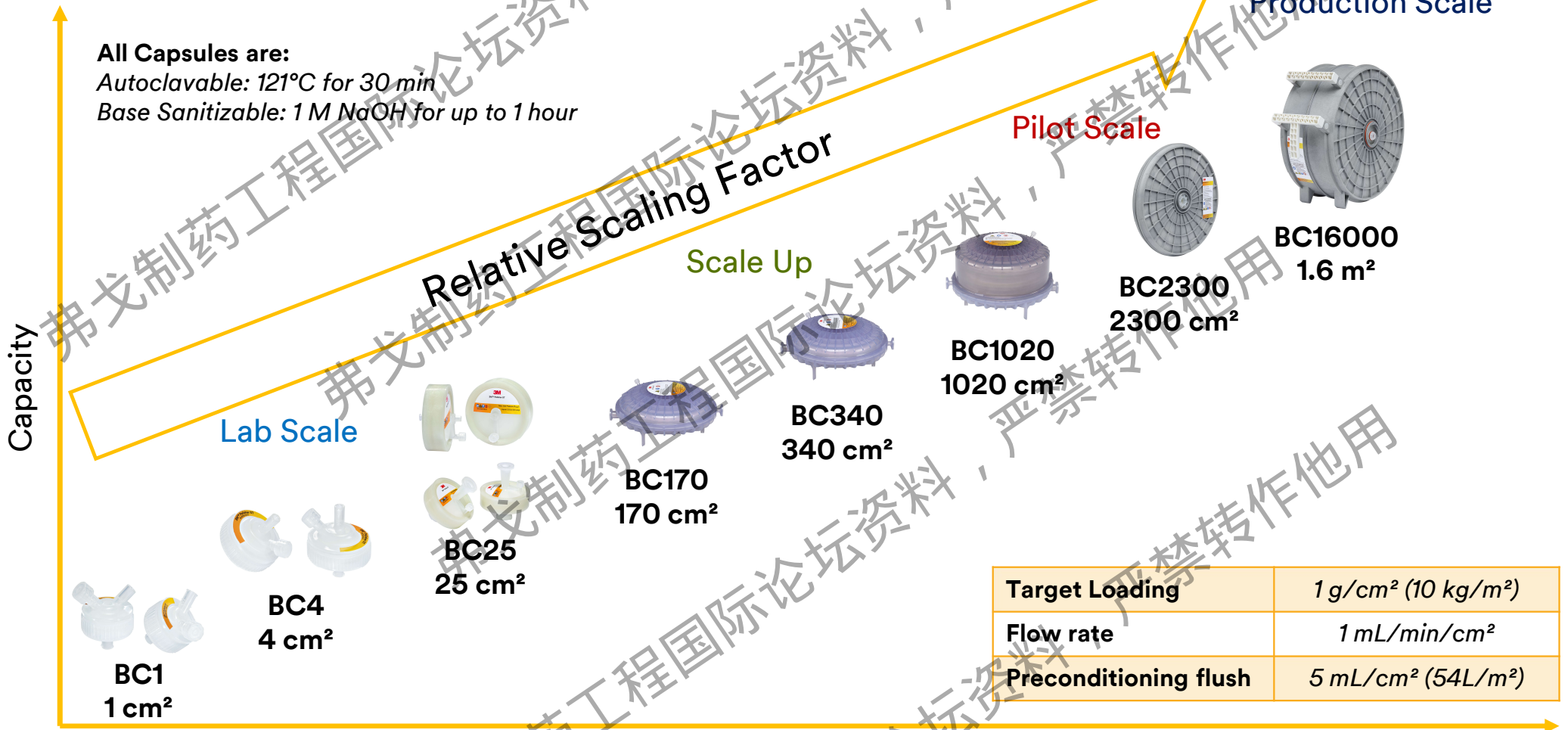
3M™ Polisher ST

Capsule Sizes and Scaling

All Capsules are:

Autoclavable: 121°C for 30 min

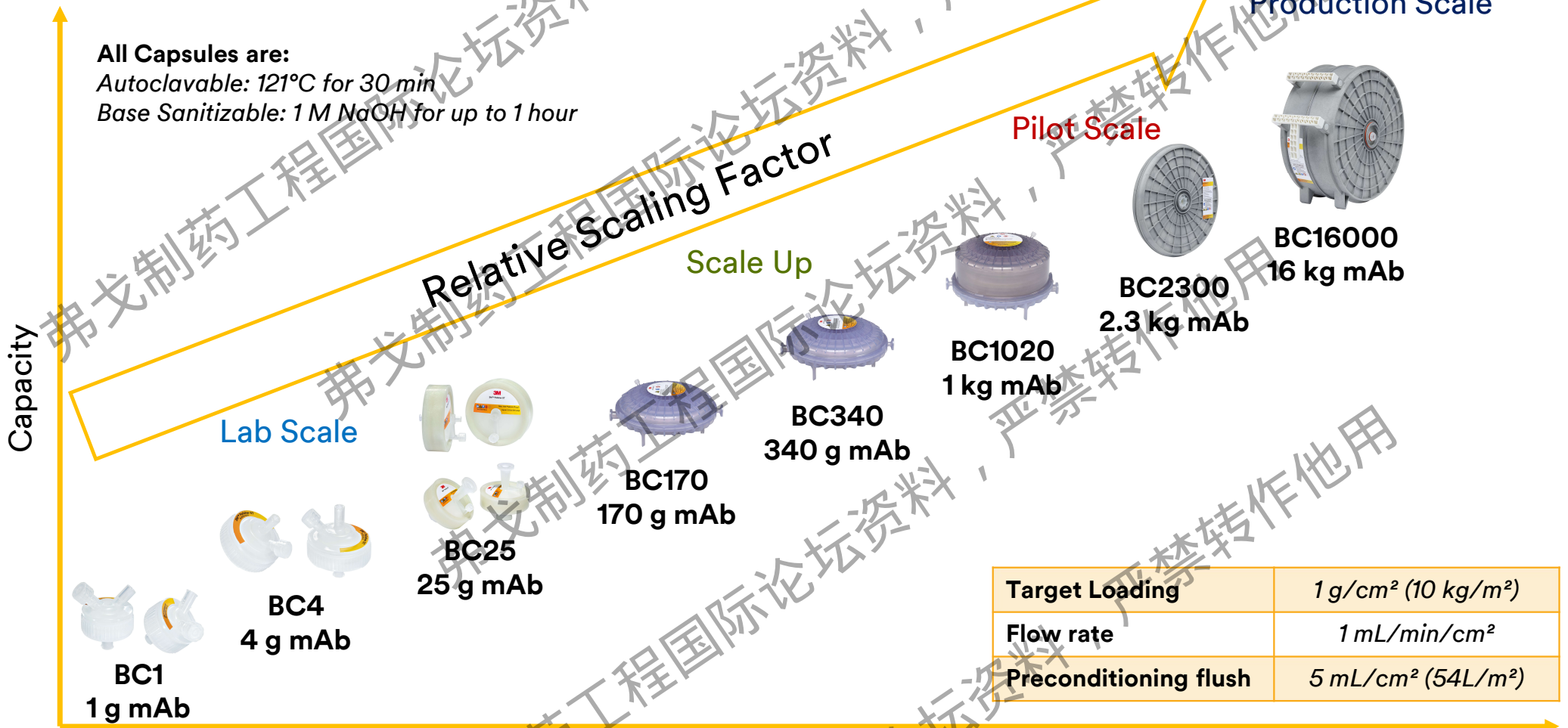
Base Sanitizable: 1 M NaOH for up to 1 hour



Target Loading	1 g/cm ² (10 kg/m ²)
Flow rate	1 mL/min/cm ²
Preconditioning flush	5 mL/cm ² (54L/m ²)

3M™ Polisher ST

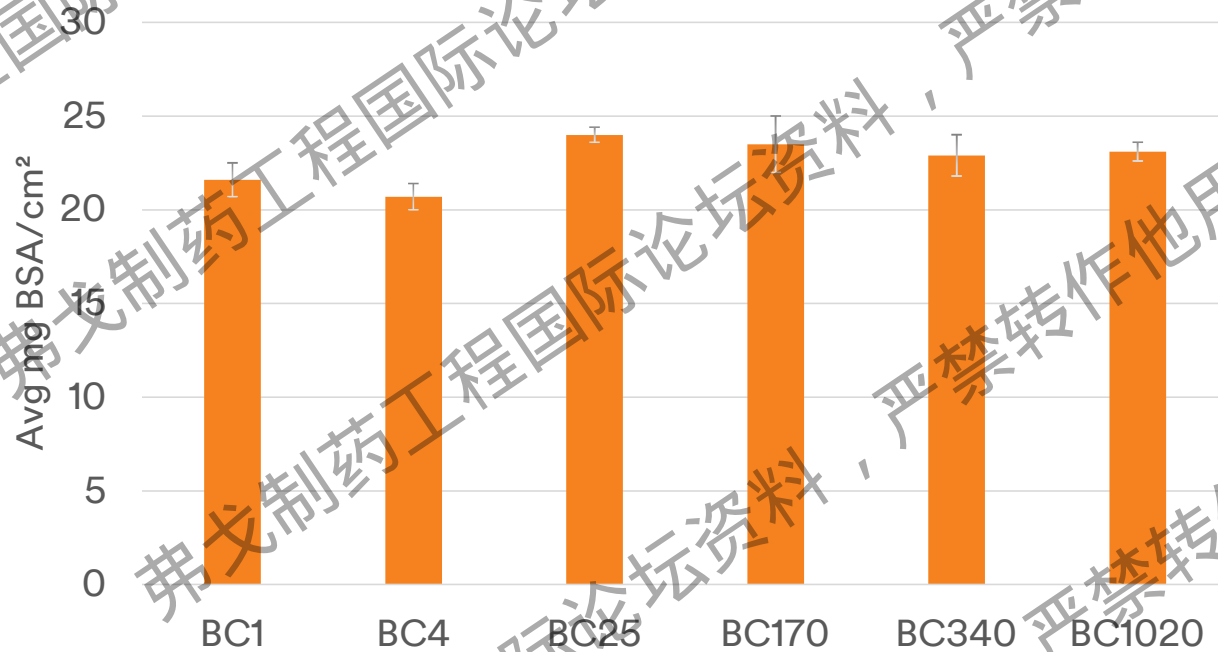
Capsule Sizes and Scaling



Robust scaling with consistent capacity

Bovine serum albumin (BSA) dynamic binding capacity (DBC) using a 1 mg/mL solution in 50 mM Tris, pH 8, 50mM NaCl (~6 mS/cm) at 1 mL/min/cm²

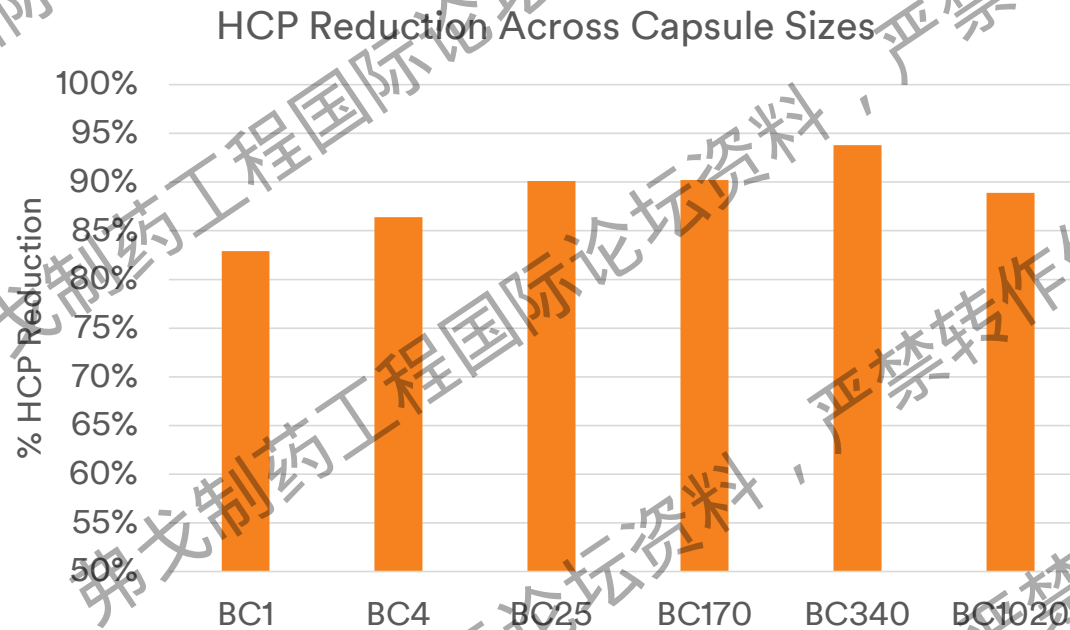
BSA DBC at 10% Breakthrough



Capacity scalability across all capsule sizes up to BC1020

Robust scaling with consistent capacity

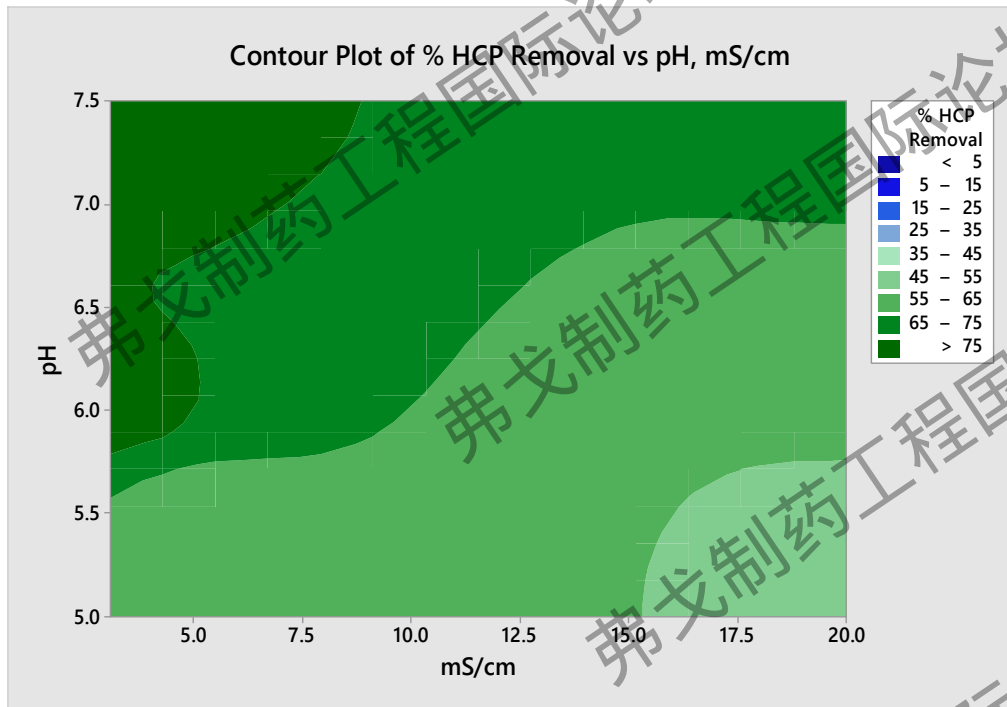
50mM Tris buffer, pH 7.5, 5 mS/cm spiked with HCP to a concentration of 10 µg/mL.
Target loading was 500 µg/cm² which simulates a 500 ppm HCP solution loaded to 10 kg/m².



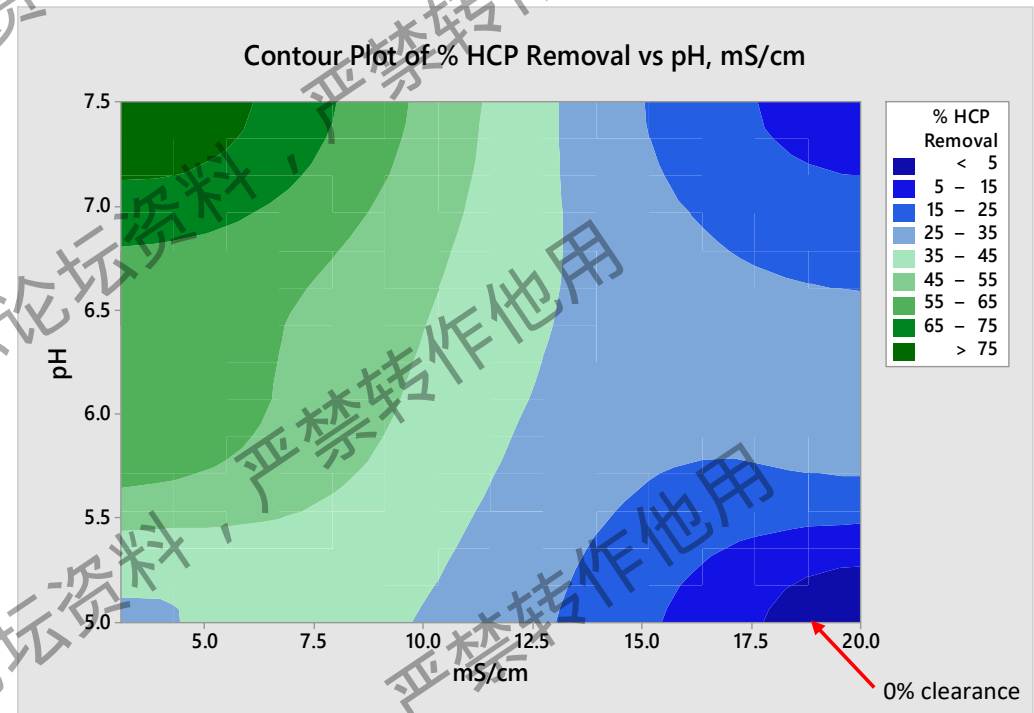
HCP reduction scales across all capsule sizes.

HCP removal across wide range of conditions

3M™ Polisher ST (10 kg/m²)



Q Chemistry (200 g/L)

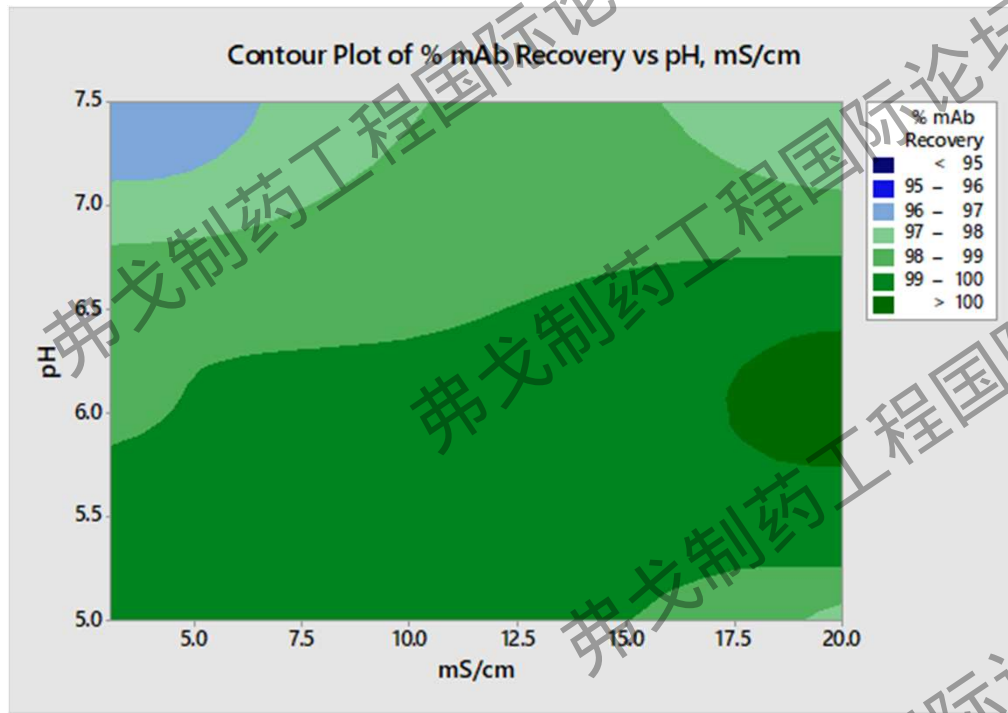


~500 ppm HCP in a VIN mAb pool (Tris/Acetate)

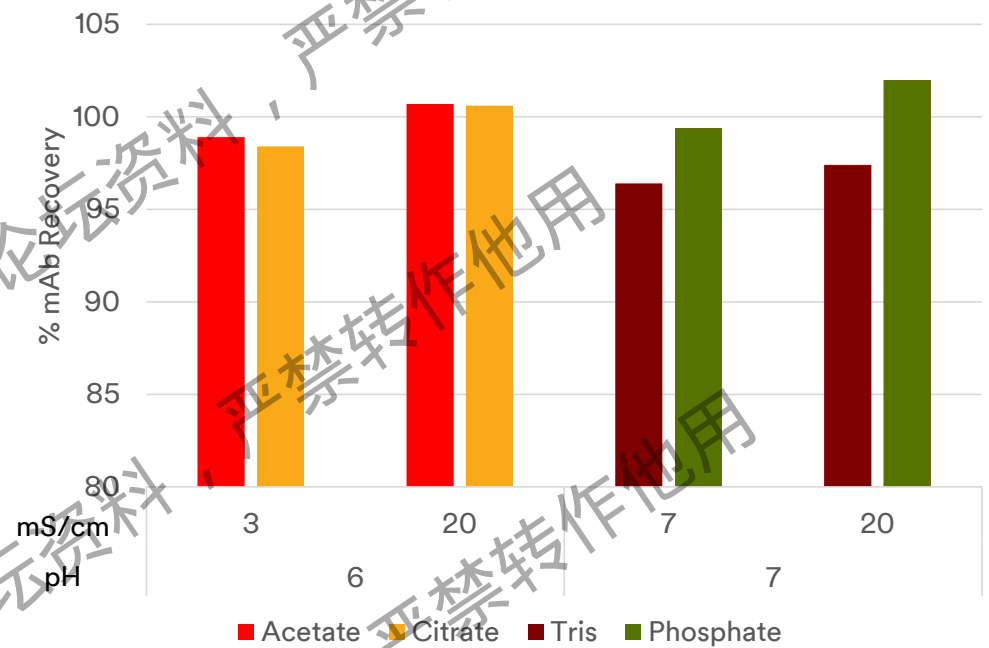
> 50% HCP removal for 3M™ Polisher ST between pH 5 and 7.5 and 3-20 mS/cm

Excellent mAb recovery

3M™ Polisher ST (10 kg/m²)
Acetate/Tris



% mAb Recovery in Monovalent and Polyvalent Buffers

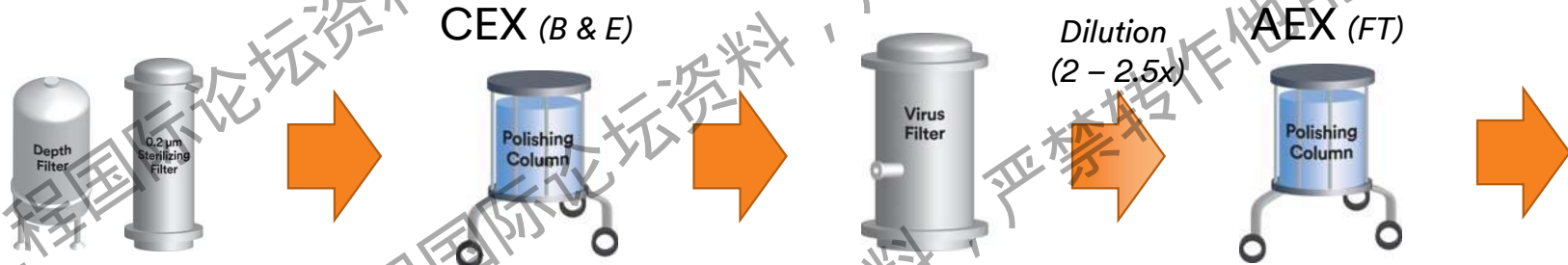


~500 ppm HCP in a VIN mAb pool

> 95% recovery at all conditions in monovalent and polyvalent buffers

Polishing Trains in mAb Production

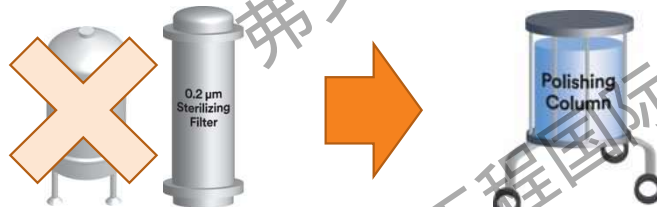
Legacy



Modern



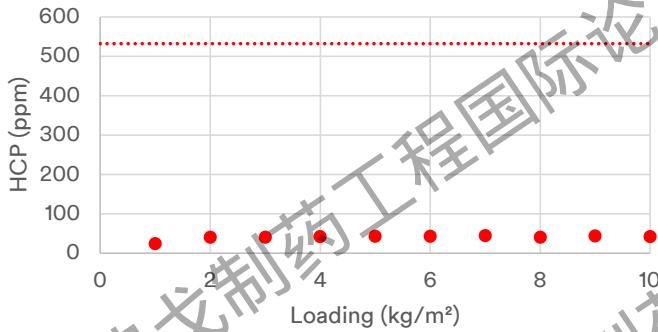
Next gen



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

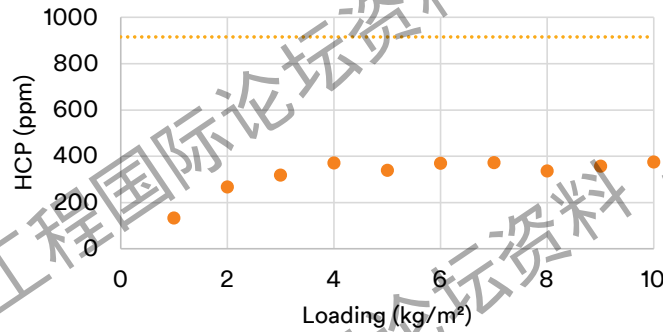
HCP Removal from 6 Model mAb Streams

CONDITION #1: pH 7.5 & 5 mS/cm
(Tris)



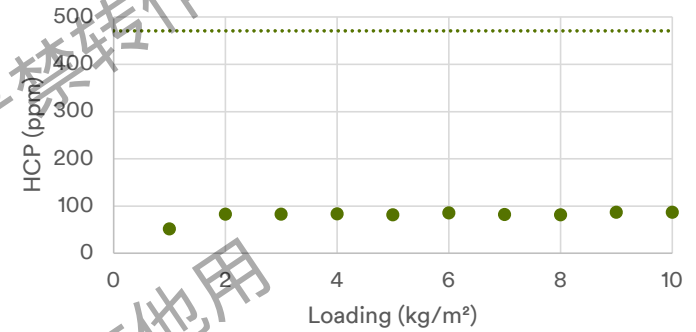
Legacy

CONDITION #3: pH 5.5 & 5 mS/cm
(Acetate)



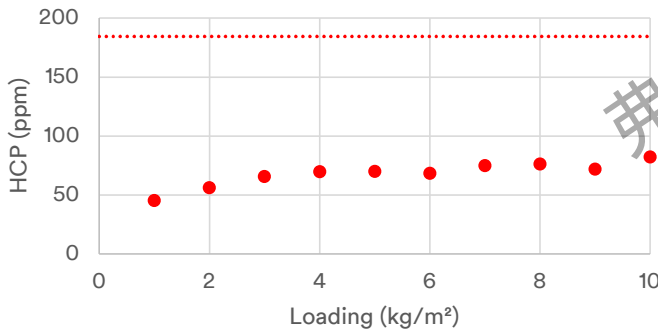
Modern

CONDITION #5: pH 7.0 & 7 mS/cm
(Tris)

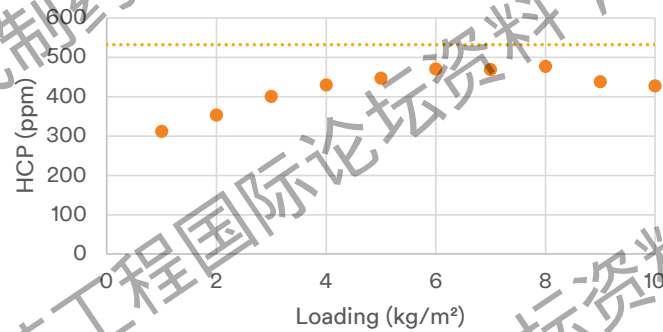


Next gen

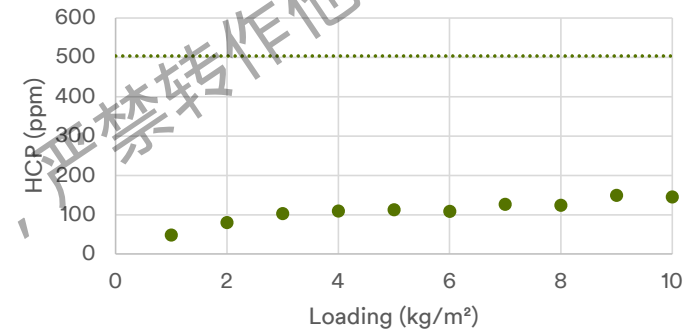
CONDITION #2: pH 7.5 & 20 mS/cm
(Phosphate)



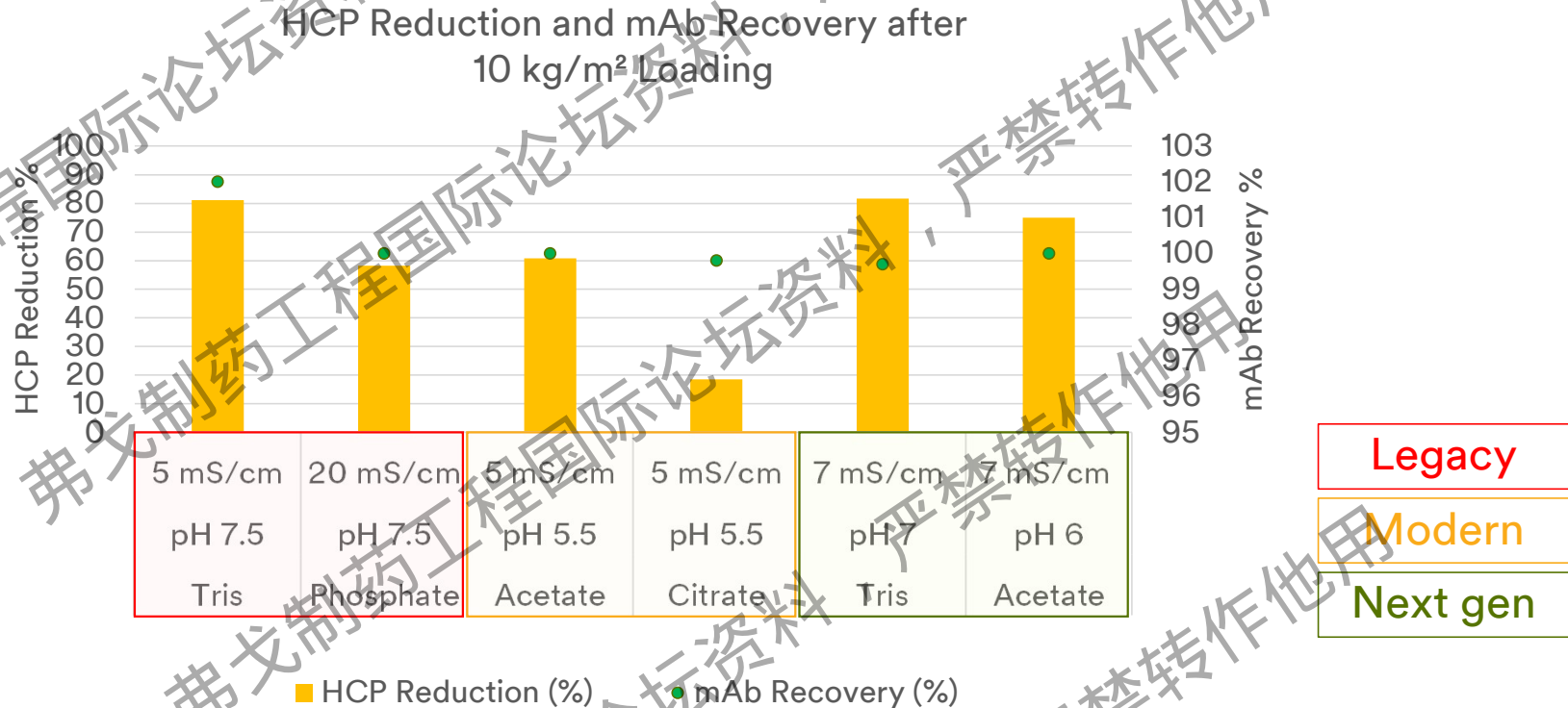
CONDITION #4: pH 5.5 & 6 mS/cm
(Citrate)



CONDITION #6: pH 6.0 & 7 mS/cm
(Acetate)



HCP Removal from 6 Model mAb Streams



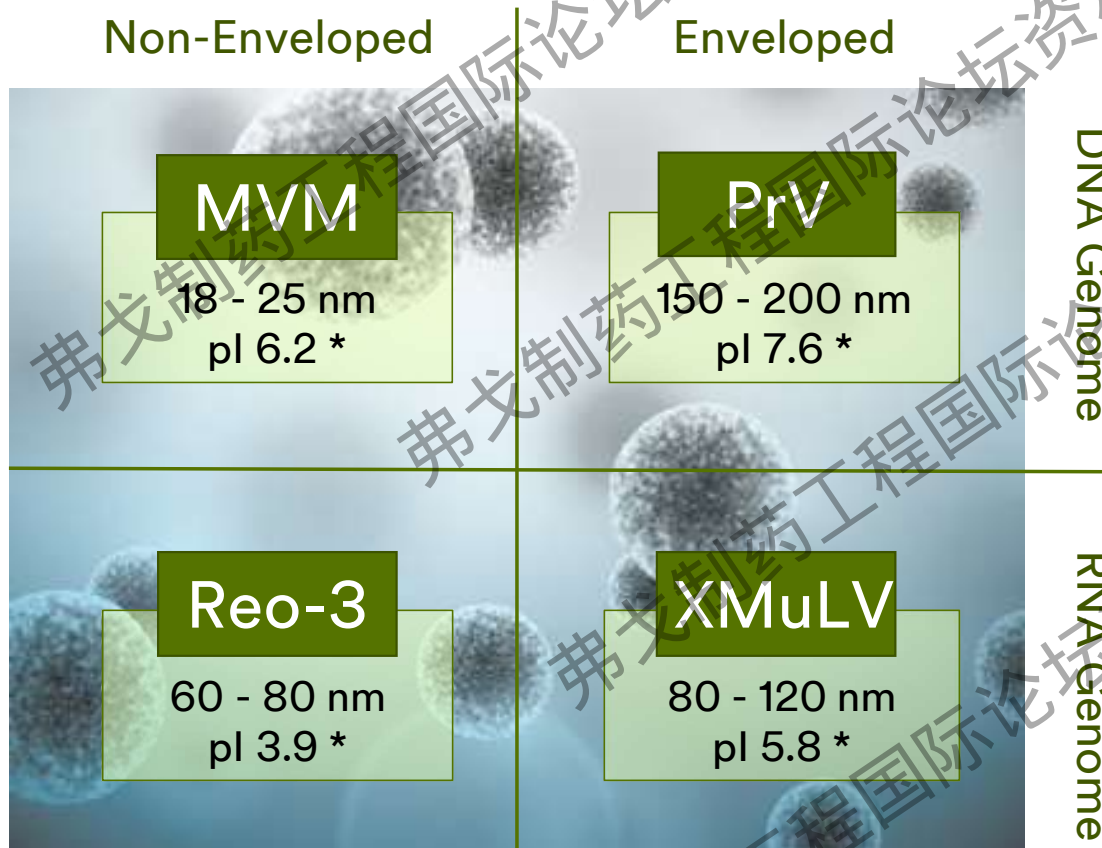
> 50% HCP Reduction for conditions other than citrate

> 99% mAb recovery was shown

DNA reduction from 20-1000 ppb to Detection Limits (data not shown)

Viral Clearance

Standard viral clearance panel for CHO cultures

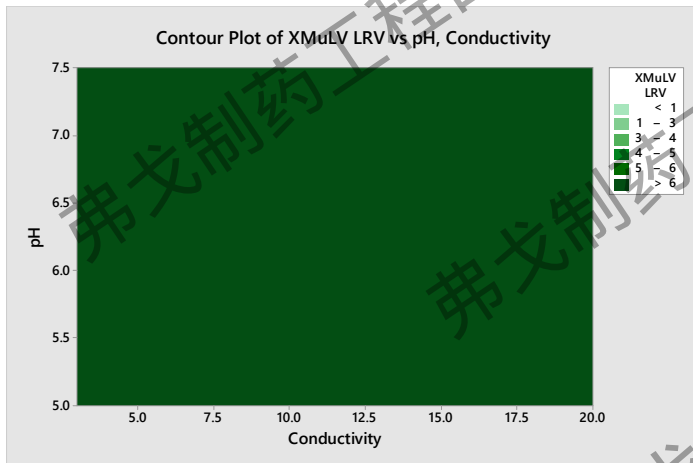


Virus	Abbreviation	Family	Hydrophobicity rank*
Xenotropic murine leukemia virus	XMuLV	Retrovirus	3
Reovirus 3	Reo-3	Reovirus	2
Pseudorabies virus	PrV	Herpesvirus	4 (highest)
Minute Virus of Mice	MVM	Parvovirus	1 (lowest)

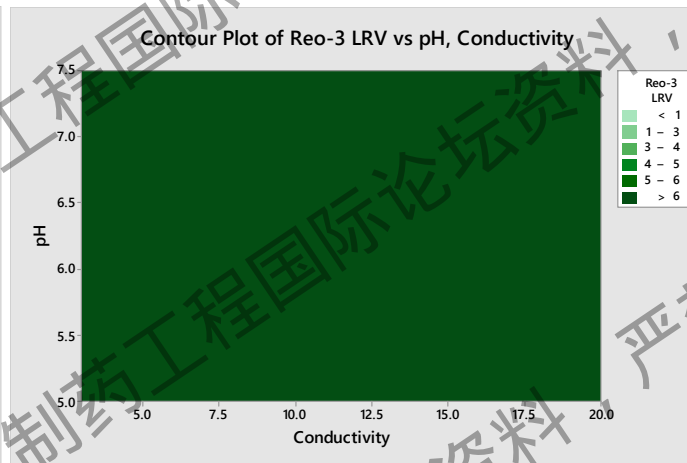
*Values from Brown, MR et al; Biotechnol Prog. 2018 Jul;34(4):1019-1026. Note that pI values can be highly variable and are more for illustrative purposes. For instance we had previously seen MVM with a pI of 5-5.3

Robust viral clearance in buffer

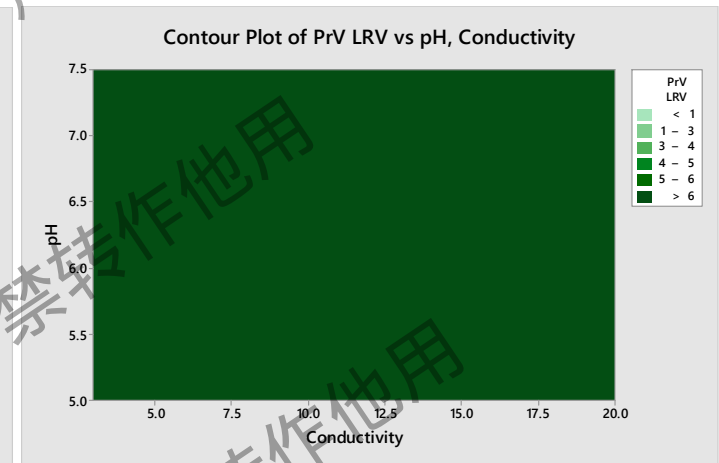
XMuLV



Reo-3



PrV



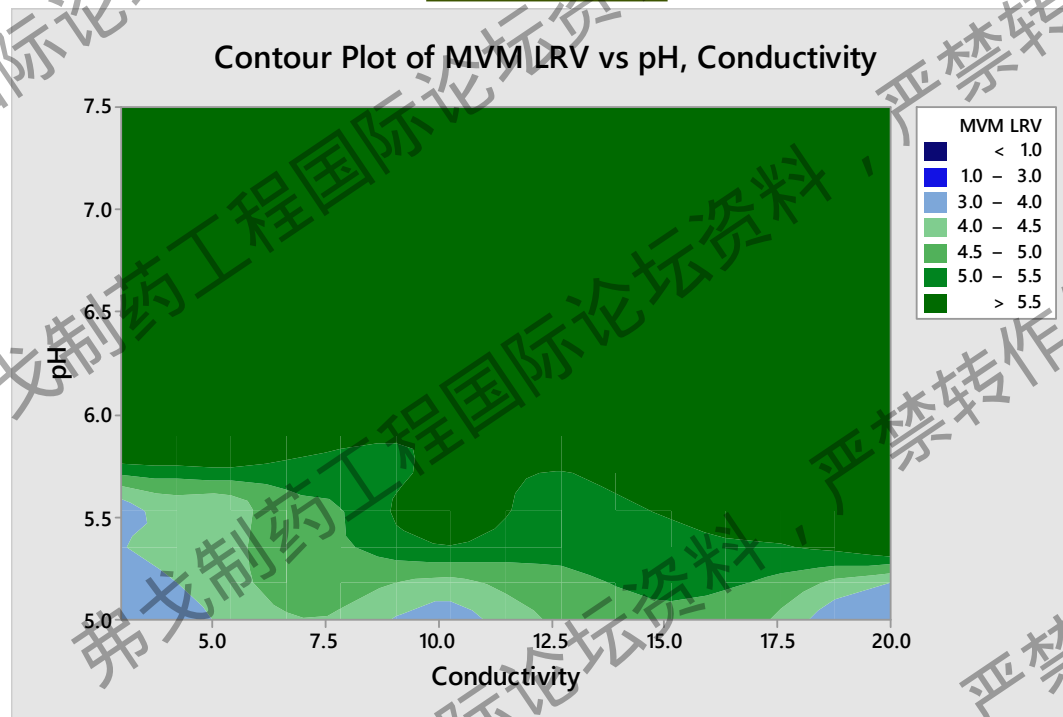
Viral Clearance Studies performed at Texcell

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

Robust viral clearance in buffer

MVM

Viral Clearance Studies performed at Texcell



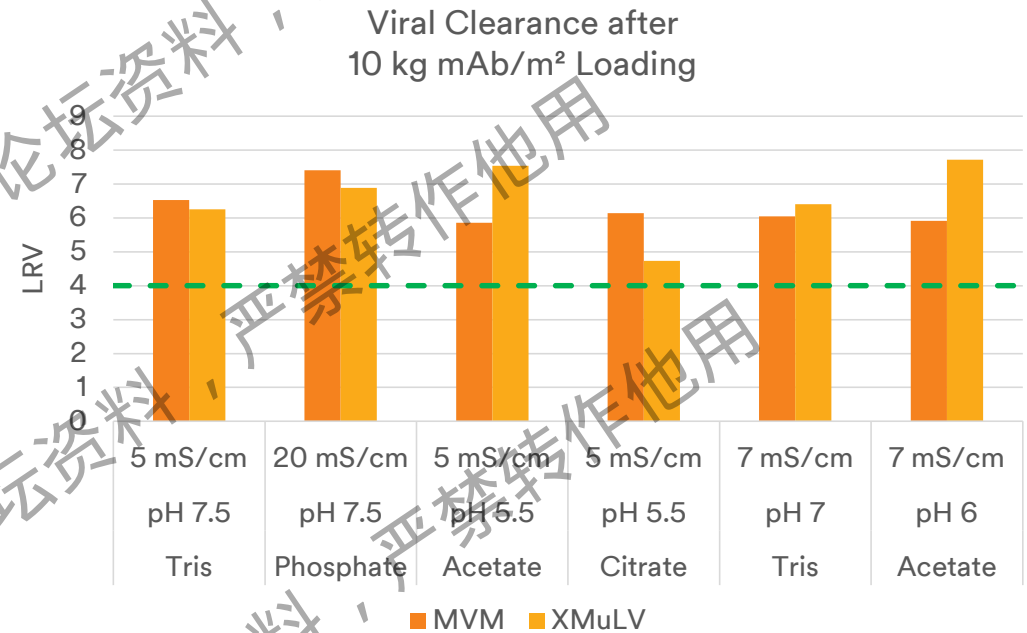
MVM showed > 4 LRV clearance from pH 5.5 - 7.5, conductivities 5 - 20 mS/cm and in both monovalent (Acetate/Tris) and polyvalent (Citrate/Phosphate) buffers

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.

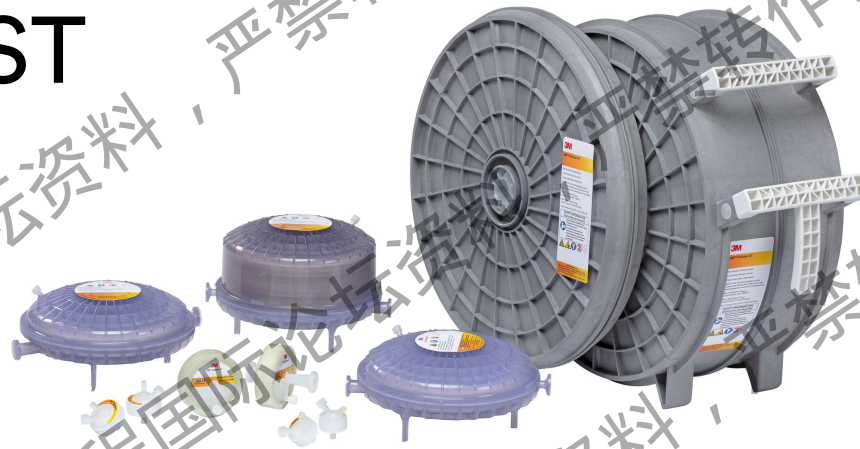
Feed Stream	Buffer	pH	Cond. (mS/cm)	Turbidity	Target HCP (ppm)	Target DNA (ppb)
Legacy	Tris	7.5	5	no	200	20
Legacy	Phosphate	7.5	20	no	200	20
Modern	Acetate	5.5	5	yes	500	1000
Modern	Citrate	5.5	5	no	500	50
NextGen	Tris	7.0	7	no	500	50
NextGen	Acetate	6.0	7	no	500	50



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

3M™ Polisher ST

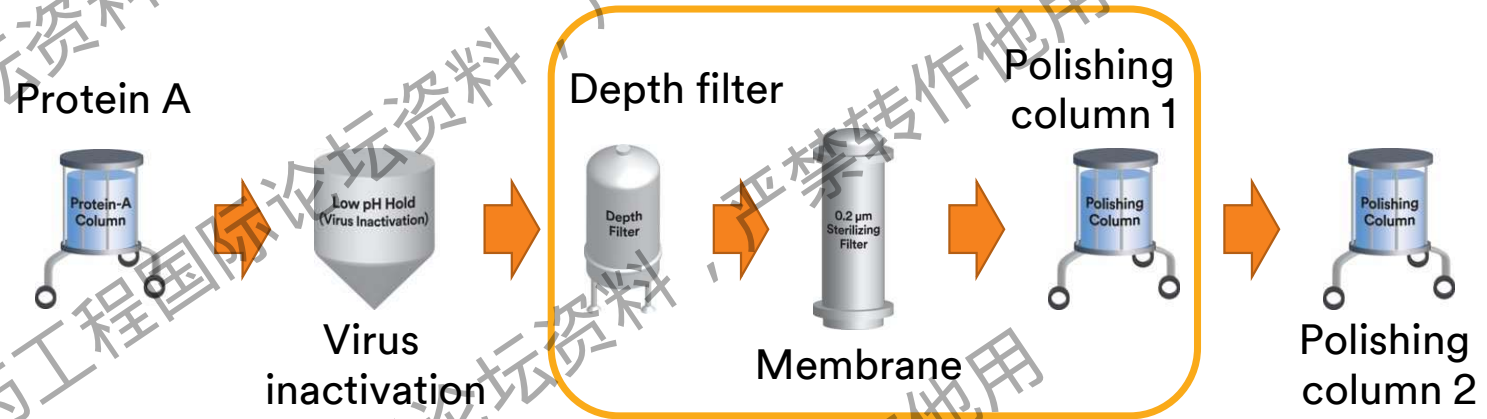
Summary



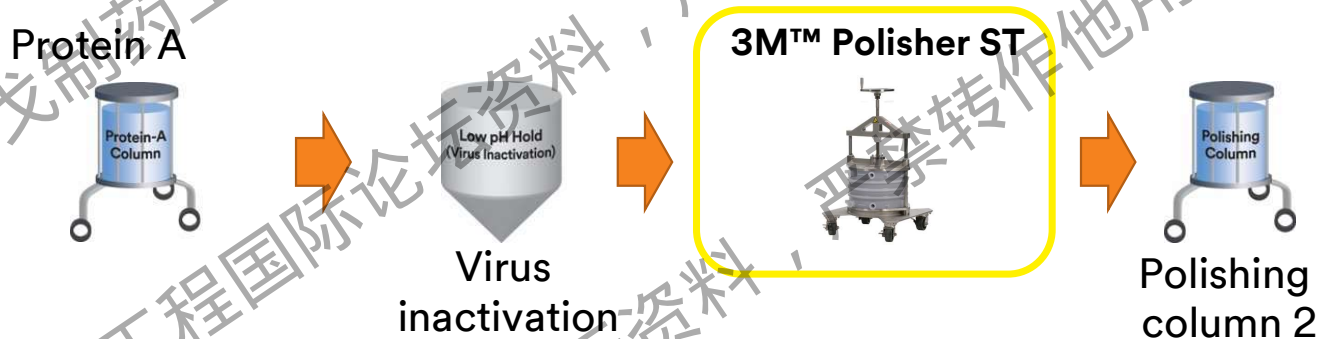
- ❑ **> 100x mAb loading of typical Q resin :** *10+ kg/m² target loading*
- ❑ **Scalability from lab to manufacturing scale :** *1 g (BC1) – 16 kg (BC16000)*
- ❑ **High salt and low pH tolerance :** *> 50% HCP reduction from pH 5 - 7.5, 3 - 20 mS/cm*
- ❑ **Robust viral clearance across very wide range of conditions :** *4 LRV from pH 5.5 - 7.5, 5 - 20 mS/cm in Acetate, Citrate, Phosphate and Tris Buffers*
- ❑ **Ability to perform in presence of turbidity :** *Ability to process feed streams of 40 NTU with no increase in pressure & removing turbidity*

Simplification of the polishing train

Traditional process:



Simplified process:



Thank You

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