Science.
Applied to Life.™

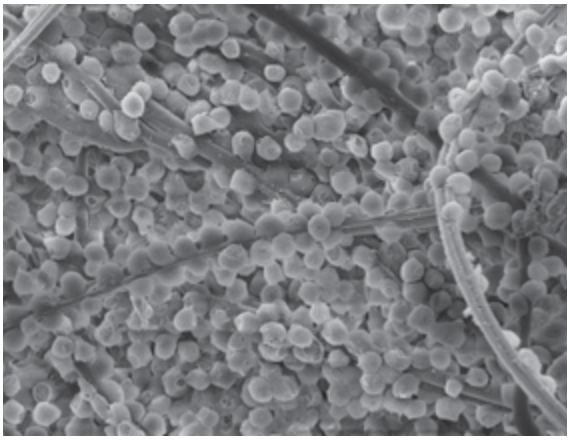

# 3M™ Harvest RC

**Single-stage chromatographic purification for recombinant protein therapeutic manufacturing.**

# Advancing harvest technology.

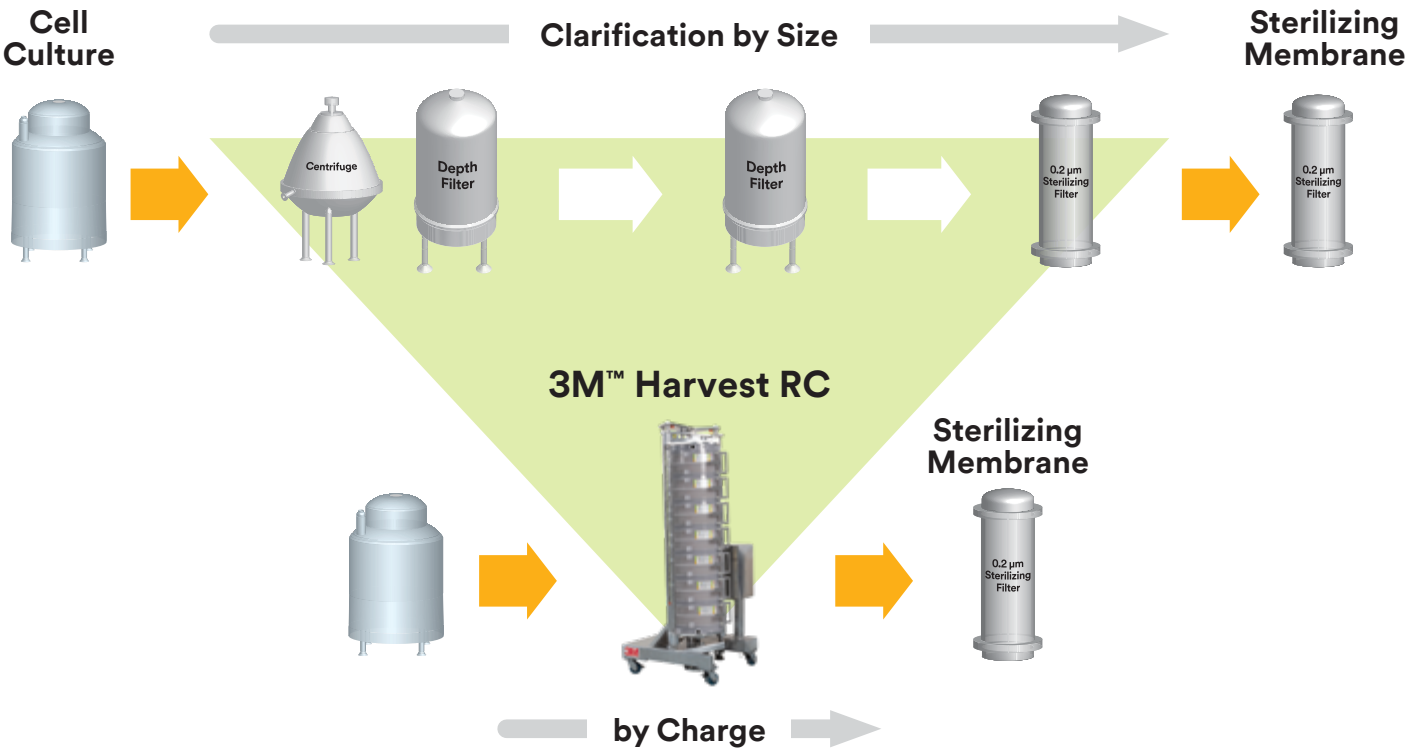
The first step in the recombinant biotherapeutic process is harvesting cell culture fluid containing the product. Conventional approaches for performing this unit operation utilize a combination of depth filtration, centrifugation, and membrane filtration. These technologies utilize differences in density and in size as the principles of separation. As cell culture processes are intensified to yield higher cell densities and product titers, the ability to effectively harvest the cell culture fluid with the consistency and scalability required becomes challenging.

3M™ Harvest RC is a harvest solution that utilizes fibrous anion exchange (AEX) chromatography to efficiently separate the cells, cell debris, and DNA from the harvest fluid containing the target product. Precision quaternary ammonium (Q) functionalized polypropylene fibre, combined with a 0.2 µm PES membrane, provides scalable and predictable clarification from discovery to commercial manufacturing scale.



*Cells being captured by AEX fibre chromatography*

## Single-stage harvest and clarification.




*Simplify three stages into a single stage.*

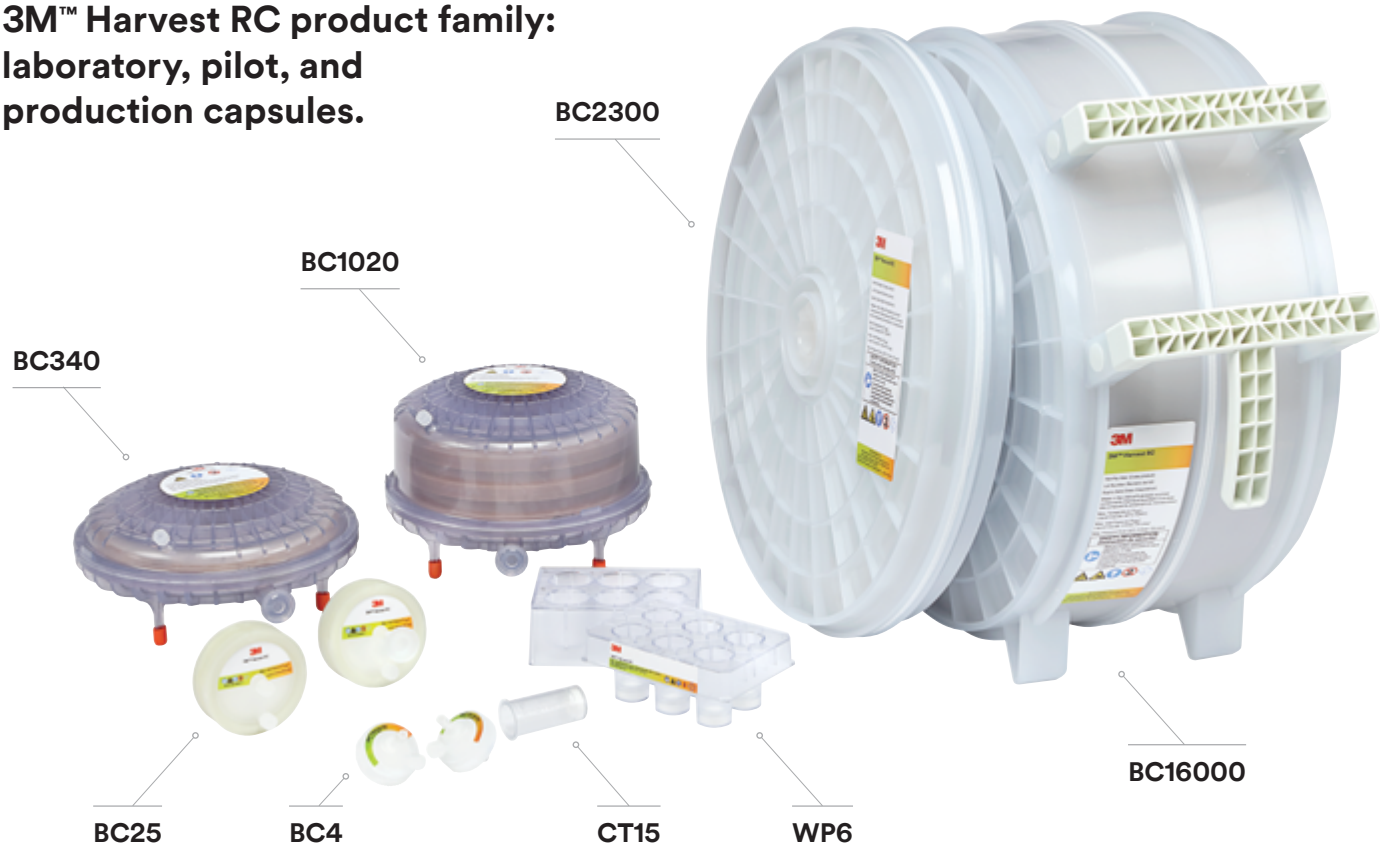
# Introducing 3M™ Harvest RC.

A new single-step, single-use chromatographic clarification solution, the 3M™ Harvest RC is the next generation in harvest and clarification technology. It is designed as an efficient option to increase monoclonal antibody (mAb) yields while streamlining the upstream process by replacing the centrifuge and/or depth filtration process steps.

- Capsule format enables typical product recoveries of 95+%
- Replaces primary, secondary, and guard membrane clarification stages
- Predictably scales from discovery to manufacturing in terms of clarification consistency and cell loading capacity
- Capsules fit into laboratory to manufacturing scale workflows
- Lower total cost of manufacturing compared to centrifugation and depth filtration
- No post-use cleaning required which means that there is no use of caustic or potentially toxic clean-in-place (CIP) agents
- Lower consumption of buffer and water compared to depth filtration

Discovery | Development | Scale-up | Manufacturing

## 3M™ Harvest RC product family: laboratory, pilot, and production capsules.



# Innovative design and performance.

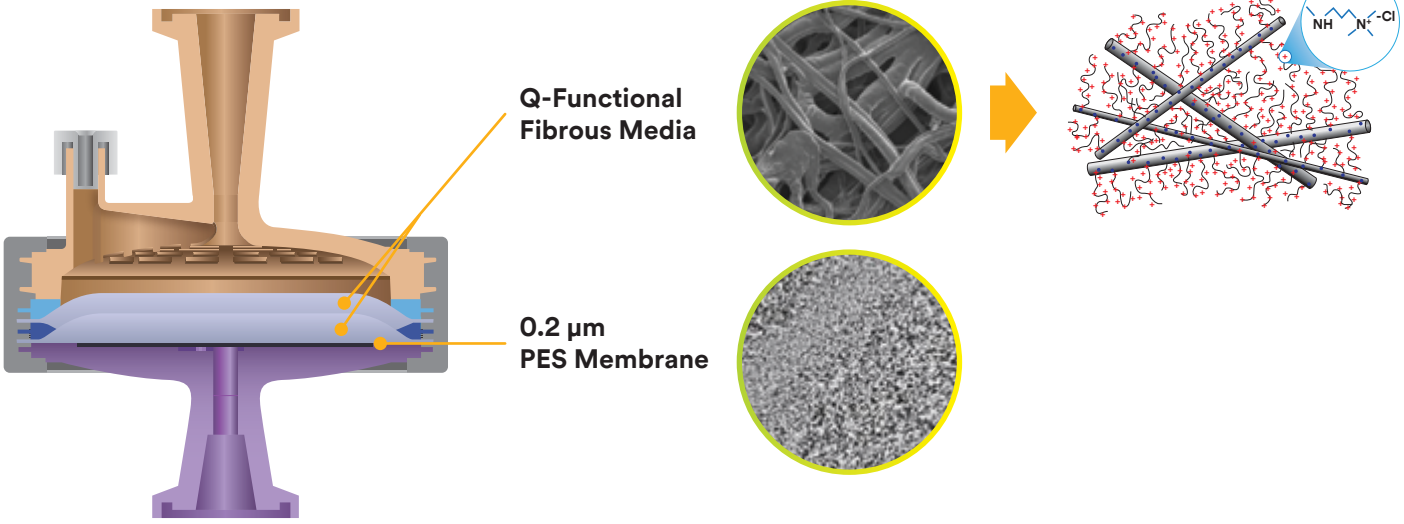
3M™ Harvest RC encapsulates innovative synthetic fibrous anion exchange (AEX) chromatography media and a 0.2 µm polyether sulfone (PES) membrane. This enables a single-stage clarification process of low to high-density cell culture (>40 million cells per mL) with high recovery, and high fidelity of soluble and insoluble contaminant separation.

Cells are bound inside the media by electrostatic charge interaction with the AEX chromatographic fibres. This results in the efficient retention of large and small particulates without developing a surface cake layer. The media can also help remove soluble impurities which results in cleaner effluent than centrifugation or depth filtration.

- High mAb product recovery (Capsules: >95%; Conical Tube and Well Plate >90%)
- Consistent cell loading capacity
- Turbidity reduction (<15 NTU)
- DNA reduction (<500 ppb)
- Minimal cell shear
- 0.1 µm sterile filter protection

**Before and after using 3M™ Harvest RC: turbidity reduction in a single stage**

## Expanding fibrous media platform.




## Available formats:

**Well plate**

**Conical tube**

**Laboratory scale**

# Performance Data

## mAb product recovery.

3M™ Harvest RC is a single stage chromatography solution that effectively clarifies Chinese Hamster Ovary (CHO) harvest cell culture fluid (HCCF) across a wide range of cell densities, packed cell volumes (PCV), and turbidities.

3M™ Harvest RC chromatographic clarification capsules consistently provide >95% mAb product recovery for high cell density cultures from the laboratory to the manufacturing scale.

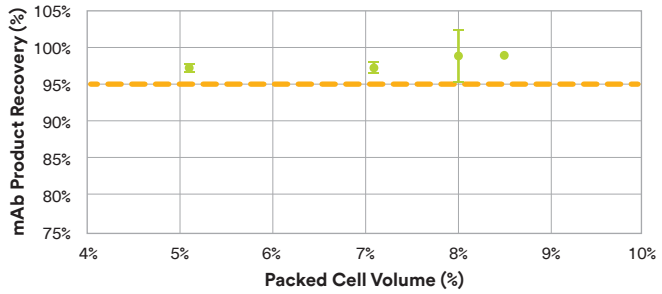



**Figure 1A:** mAb product recovery in clarification process at different packed cell volumes (N = 1 – 4)

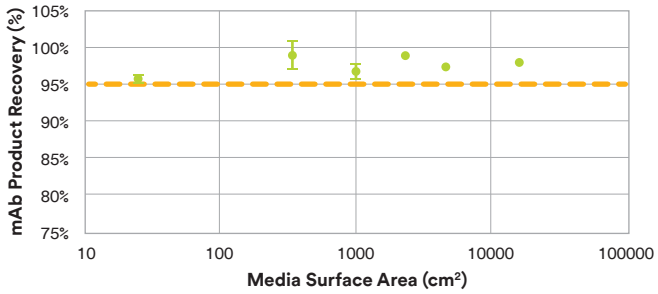



**Figure 1B:** mAb product recovery in clarification process at different media surface areas (N = 1 – 3)

## Turbidity reduction.

3M™ Harvest RC provides consistent separation of cells, cell debris, and DNA from the target protein. Clarified cell culture fluid (CCCF) has low turbidity, typically <15 NTU. Additionally, consistently low acidified turbidity of CCCF indicates significant reduction of DNA in the clarified material. Low acidified CCCF turbidity is a measure of the amount of DNA present in the cell culture fluid. (Koehler et al. Biotechnology Progress. 2019;35:e2882)

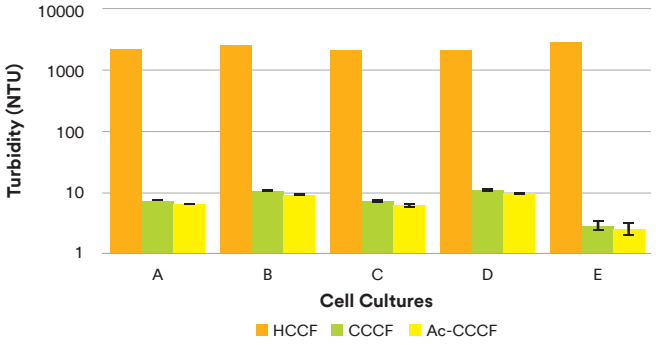



**Figure 2:** Turbidity Reduction by 3M™ Harvest RC capsules (N = 3 – 6). A – E are different CHO cell cultures at 5 – 8% PCV.

## Scalability.

3M™ Harvest RC capsules scale linearly across laboratory, pilot, and manufacturing scales.

Fibrous chromatographic clarification assures scalable performance from discovery to manufacturing scales. Performance is consistent from laboratory capsules (BC4 and BC25), scale-up capsules (BC340 and BC1020), to production capsules (BC2300 and BC16000) within ±20% of BC25 throughput.

Throughputs of 3M™ Harvest RC capsules are scaled by area based on packed cell volume.

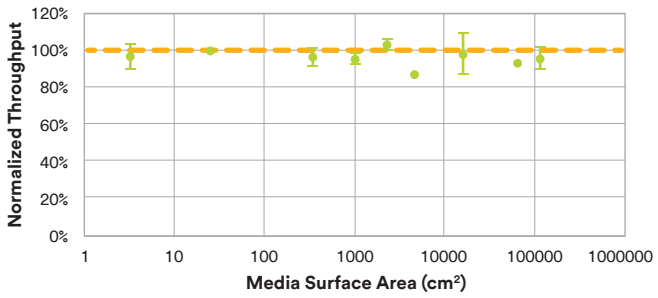



**Figure 3:** Scalability from laboratory to scale-up and production capsules (N = 1 – 5, 6 cell cultures)

## Cell loading capacity.

Utilizing an advanced Q functionalized fibrous chromatography media to achieve single-stage clarification, 3M™ Harvest RC enables predictable and consistent cell loading capacity for CHO cell culture fluid for a wide range of packed cell volumes.

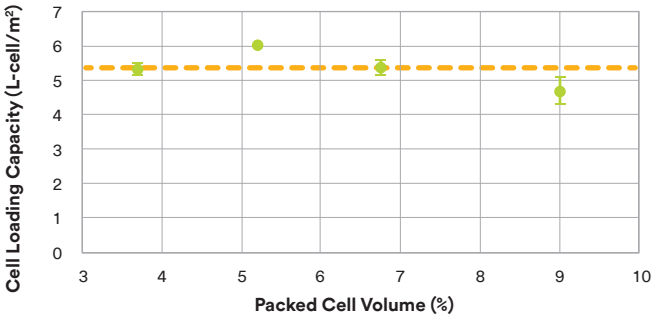



**Figure 4:** Cell loading capacity of 3M™ Harvest RC capsules for CHO harvested cell culture fluid at different packed cell volumes (N = 2 - 3)

## Cell shear.

The low-pressure chromatographic clarification relies on charge rather than size or density. This results in minimal cell shear compared to conventional depth filtration processes even at medium and high cell densities. Cell shear was evaluated by lactate dehydrogenase (LDH) assay (Sigma-Aldrich 11644793001).

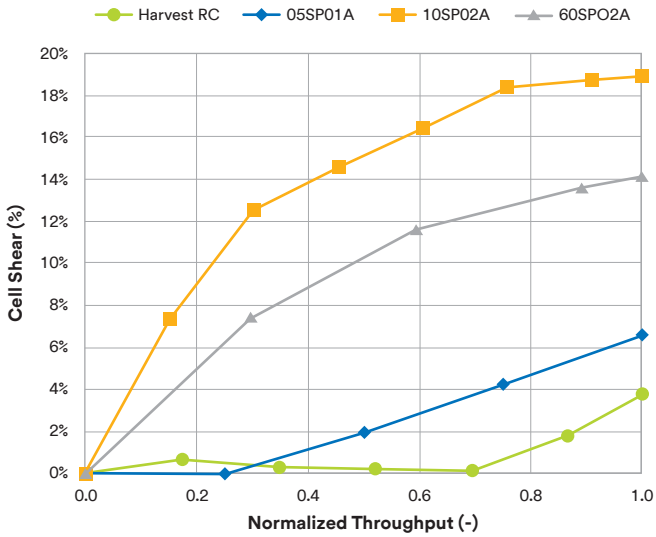



**Figure 5:** Minimal cell shear of 3M™ Harvest RC during clarification of 8% PCV CHO cell culture at 100 LMH.

## Robust sterile filter protection.

Due to the highly effective chromatographic reduction of soluble and insoluble contaminants, 3M™ Harvest RC enables efficient clarification, and is capable of effective protection of final sterilizing grade membrane filter down to 0.1 µm pore size.

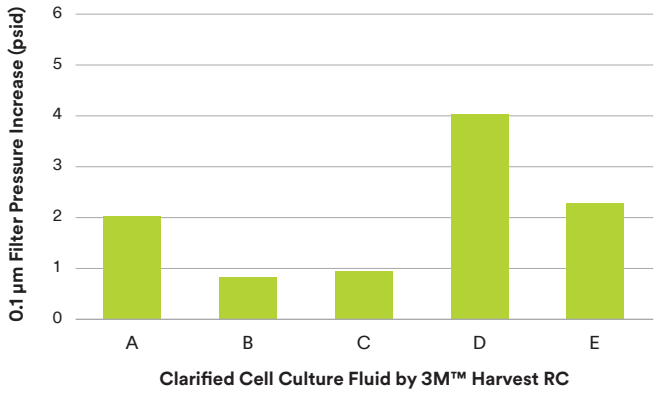
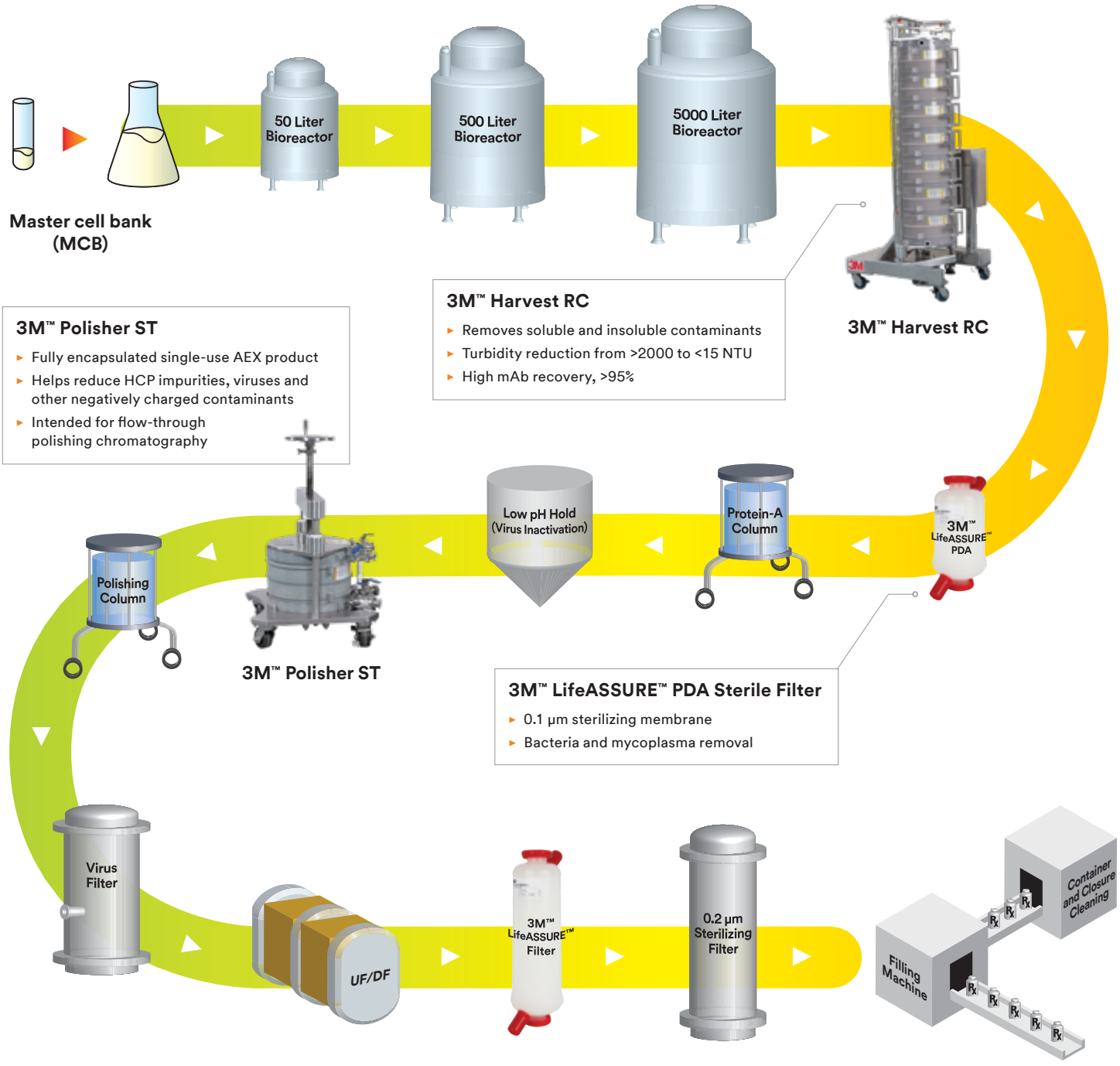



**Figure 6:** 0.1 µm sterile filter pressure increase at 500 L/m². A – E are clarified fluids of CHO harvested cell culture fluids at 8%PCV by 3M™ Harvest RC capsules.

# Biopharmaceutical Purification Process Improvements

This process train illustrates the potential of combining 3M products that work together to create an intensified manufacturing process, eliminating several process steps.

## Cell harvest simplified.



# Ordering Guide

| Product Name | WP6 | CT15 | BC4 | BC25 Luer | BC25 Sanitary | BC340 | BC1020 | BC2300 | BC16000 |
|---|---|---|---|---|---|---|---|---|---|
| **Model Name** | EMP006HRC2FA | EMP015HRC2FA | EMP201HRC2FA | EMP301HRC2FA | EMP303HRC2FA | EMP513HRC2FA | EMP533HRC2FA | EMP710HRC2FA | EMP770HRC2FA |
| **Media Surface Area** | 2.3 $cm^2$ per well | 2.3 $cm^2$ | 3.2 $cm^2$ | 25 $cm^2$ | 25 $cm^2$ | 340 $cm^2$ | 1,020 $cm^2$ | 2,300 $cm^2$ | 1.61 $m^2$ |
| **Cell Culture Volume Range (5-8% PCV)[1]** | 15 mL per well | 15 mL | 20 - 32 mL | 150 - 250 mL | 150 - 250 mL | 2 - 3.4 L | 6 - 10 L | 14 - 23 L | 100 - 160 L |
| **Fill Volume[2]** | 15 mL per well | 15 mL | 5.6 mL | 27.6 mL | 28.2 mL | 0.66 L | 1.7 L | 3.3 L | 16.3 L |
| **Hold up Volume Post Blow Down[3]** | N/A | N/A | 3.0 mL | 12.0 mL | 12.3 mL | 0.16 L | 0.47 L | 1.1 L | 6.5 L |
| **Inlet/Outlet Connections** | N/A | N/A | Luer-Lok | Luer-Lok | Sanitary | Sanitary | Sanitary | Sanitary | Sanitary |

1. Cell Culture Volume Range is the estimation for CHO cell culture fluid at 5 - 8% packed cell volume.
2. Fill Volume is defined as the volume of liquid that is required to fill the capsule.
3. Post Blow-Down Hold-Up Volume is defined as the volume of the residual liquid after air/gas blow down.

## For more information about the **3M™ Harvest RC,** contact your local sales representative or visit us at **3M.ca/Bioprocessing**

**Intended Use:** 3M™ Harvest RC products are intended for use in biopharmaceutical processing applications of aqueous based pharmaceuticals (drugs) and vaccines in accordance with the product instructions and specifications, and cGMP requirements (for BC340, BC1020, BC2300 and BC16000) or GLP requirements (for CT15, WP6, BC4 and BC25), where applicable.

Since there are many factors that can affect a product's use, the customer and user remain responsible for determining whether the 3M product is suitable and appropriate for the user's specific application, including user conducting an appropriate risk assessment and evaluating the 3M product in user's application.

**Product Selection and Use:** Many factors beyond 3M's control and uniquely within user's knowledge and control can affect the use and performance of a 3M product in a particular application. As a result, customer is solely responsible for evaluating the product and determining whether it is appropriate and suitable for customer's application, including completing a risk assessment that considers the product leachable characteristics and its impact on drug safety, conducting a workplace hazard assessment and reviewing all applicable regulations and standards (e.g., OSHA, ANSI, etc.). Failure to properly evaluate, select, and use a 3M product and appropriate safety products, or to meet all applicable safety regulations, may result in injury, sickness, death, and/or harm to property.

**Restrictions on Use:** For CT15, WP6, BC4 and BC25: For laboratory use only. Not intended for use with materials that will be used on humans or animals. For all sizes: 3M advises against the use of these 3M products in any application other than the stated intended use(s), since other applications have not been evaluated by 3M and may result in an unsafe or unintended condition. Do not use in any manner whereby the 3M product, or any leachable from the 3M product, may become part of or remains in a medical device that is regulated by any agency, and/or globally exemplary agencies, including but not limited to: a) FDA, b) European Medical Device Directive (MDD), c) Japan Pharmaceuticals and Medical Devices Agency (PMDA) or in applications involving permanent implantation into the body; Life-sustaining medical applications; Applications requiring food contact compliance.

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