

Harvest and clarification

Harvest RC Centrate clarifier

Single-stage chromatographic clarification for centrate in recombinant protein manufacturing

This single-use, single-stage, synthetic media clarification solution uses anion exchange chromatographic technology for efficient processing of modern cell culture centrates.

Centrate clarification using Thermo Scientific™ Harvest RC Centrate Chromatographic Clarifier may provide many benefits including process compression, high product recovery, and improved process economics.

Harvest RC Centrate clarifier improves process economics:



Scalability from bench to commercial production



Predictable performance



High product recovery



Cell shear related impurity reduction



Process simplification

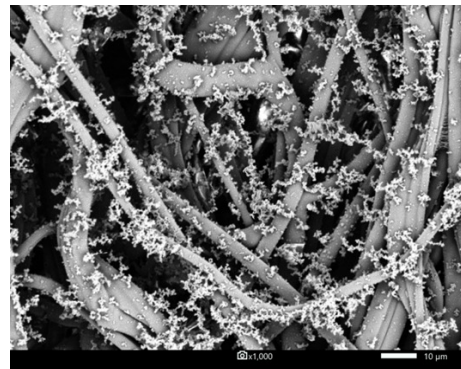


Part of the Harvest RC clarifier platform

Now you can rely on one consistent, scalable clarification platform for all development phases and process scales. The Thermo Scientific™ Harvest RC Chromatographic Clarifier platform includes Thermo Scientific™ Harvest RC Chromatographic Clarifier, for direct clarification and Thermo Scientific™ Harvest RC Centrate Chromatographic Clarifier, for centrate clarification. These innovative products provide a scalable clarification platform solution that can compress clarification process trains while providing consistent and comparable fluid quality to streamline process development and impact speed to market.

Innovative design and performance

Harvest RC Centrate clarifier encapsulates innovative synthetic fibrous anion exchange (AEX) Q-functional chromatography media combined with an asymmetric Q-functional polyamide membrane with a 0.2 μm qualifying zone. This enables effective single-stage clarification of CHO cell culture centrates produced by conventional and single-use conical plate (e.g., disc stack) centrifuges. Soluble and insoluble impurities are captured by electrostatic interactions with a positively charged ligand immobilized on fiber matrix, as well as a downstream polyamide membrane. This results in efficient retention of a wide range of particles that have not been effectively separated by centrifugation or are produced by cell shear during centrifugation. Specifically, the anion exchange mechanism enables efficient capture of impurities $<0.5 \mu\text{m}$ that are difficult to capture with traditional depth filtration and membrane filtration.



Soluble impurities captured by charged fibrous media.

Key features and benefits:

- Synthetic, functionalized fibrous media provides effective soluble impurity removal in centrate, including DNA and cell shear related sub-micron particle reduction
- Single-stage centrate clarification for process compression and streamlining of process development
- Predictable performance scalability for consistent clarification at various process scales
- High product recovery ($>95\%$) and high-capacity capsules for improved process economics
- Alkaline resistant capsules for pre-use sanitization
- Provides comparable effluent quality to Harvest RC clarifier for a modern clarification platform

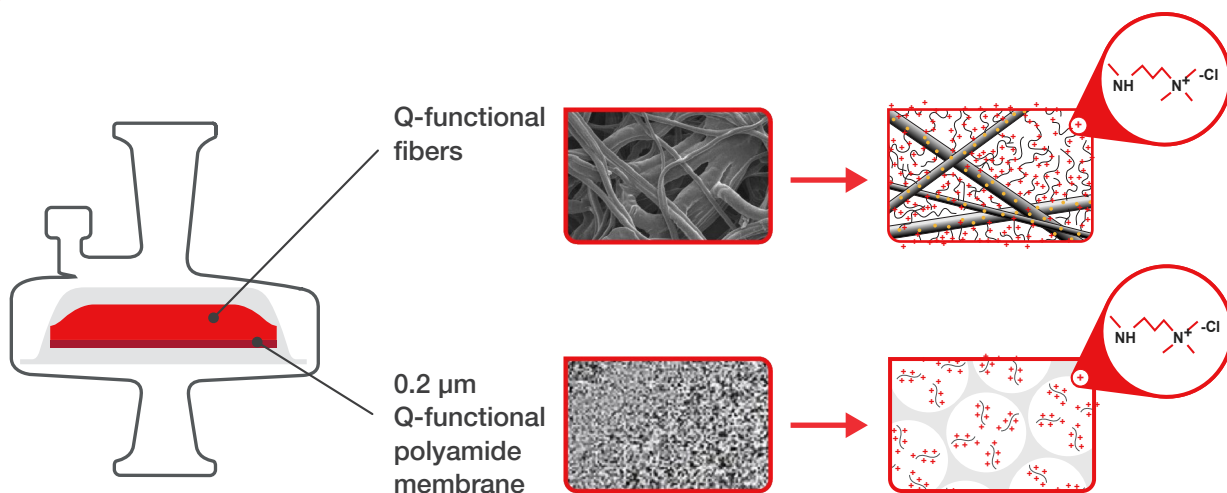


Harvest RC Centrate clarifier – Single stage chromatographic clarification encapsulated solution for centrate

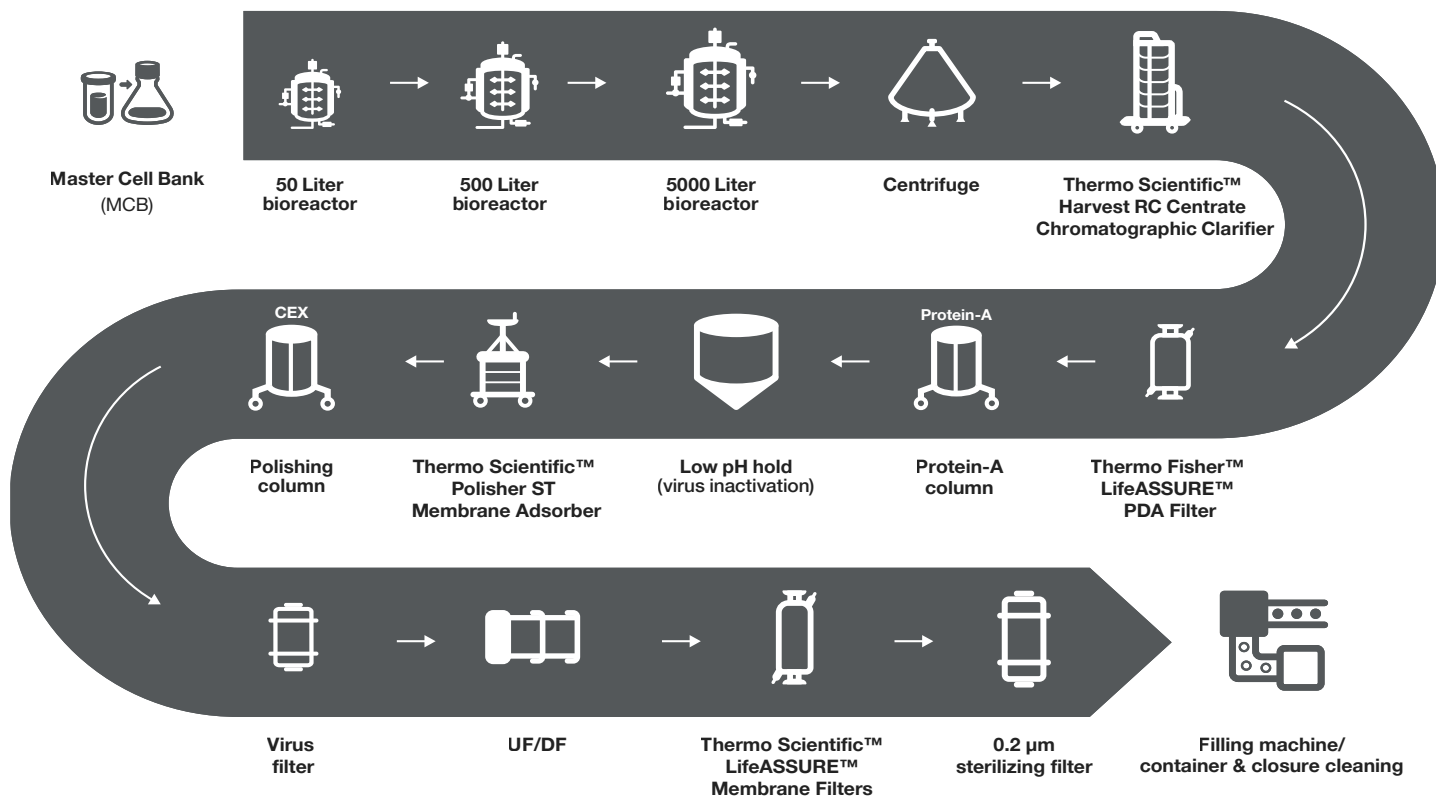
The innovative synthetic fibrous AEX chromatographic clarification media enables a single-stage centrate clarification from CHO cell cultures with high product recovery and high fidelity of soluble and insoluble impurity removal. Downstream of the fibrous chromatographic clarification media is the 0.2 µm asymmetric

Q-functional polyamide membrane which distributes the flow across the AEX media bed and enables protection of downstream sterilizing grade membrane filter. Also, the 0.2 µm functionalized polyamide membrane enables simple process endpoint measurement using pressure reading.

Expanding fibrous media platform



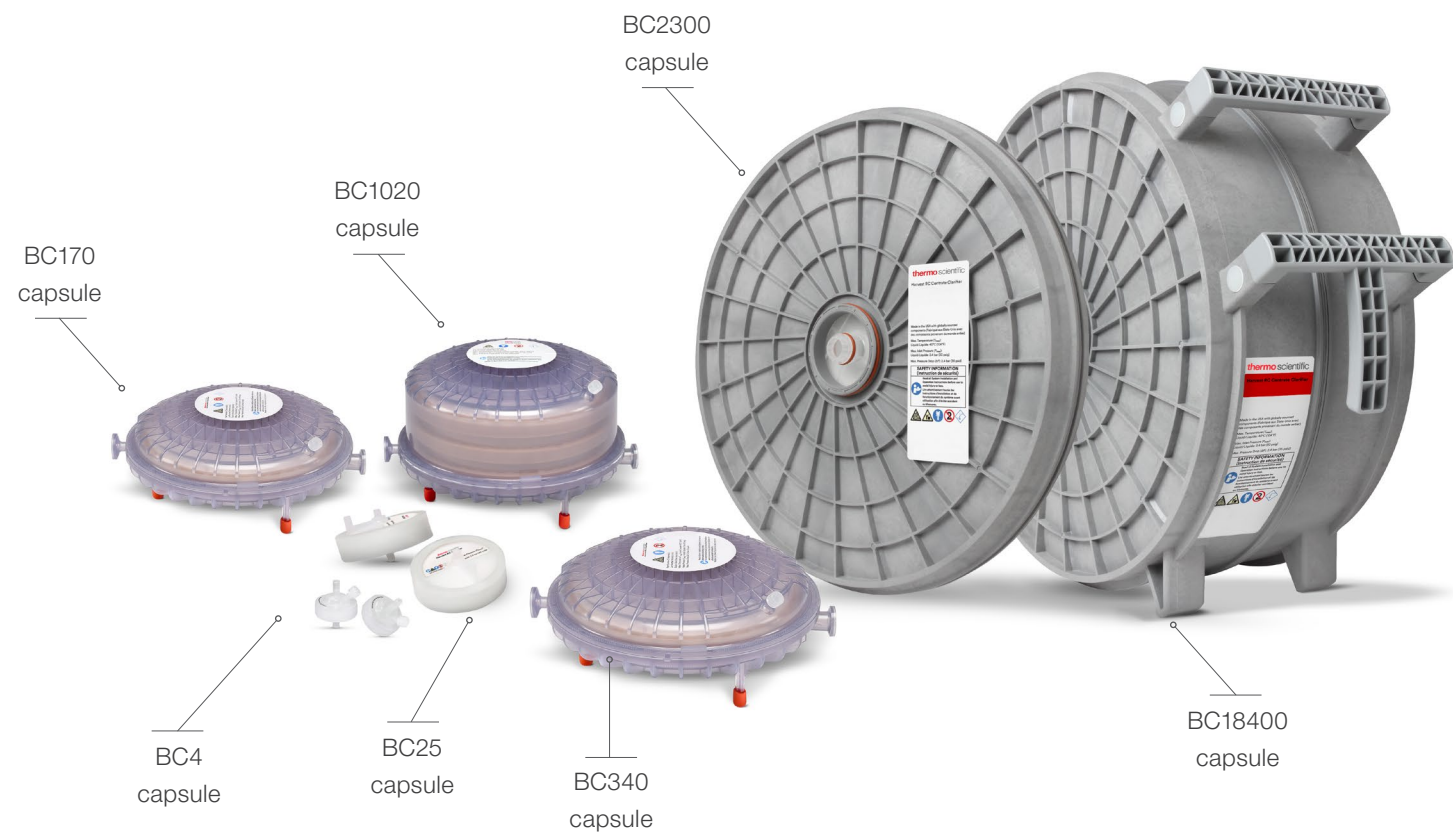
Centrate clarification simplified:



The next generation in harvest and clarification technology



Harvest RC Centrate clarifier product family:
laboratory, pilot, and production capsules



Performance data

All performance data below is based on capsules at 100 L/m²/hr flux. While it is representative of typical performance, results may vary depending on process conditions.

mAb product recovery

Harvest RC Centrate clarifier is a single-stage chromatography solution that effectively clarifies CHO cell culture centrates produced by conventional and single-use conical plate (e.g., disc stack) centrifuges. The single-mode electrostatic separation mechanism and high throughput media enables product recoveries of >95%.

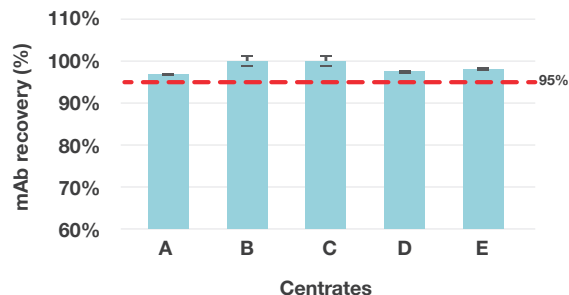


Figure 1: mAb recovery in centrate clarification with Thermo Scientific™ Harvest RC Centrate Chromatographic Clarifier. A - E are centrates from different CHO cell cultures.

Turbidity reduction

Harvest RC Centrate clarifier provides consistent separation of insoluble and soluble impurities from the target protein. Clarified centrate has low turbidity, typically <15 NTU. Additionally, low acidified turbidity of clarified centrate indicates a significant reduction of DNA in the clarified material. Low acidified centrate turbidity is a measure of the amount of DNA present in the cell culture fluid. (Koehler et al. Biotechnology Progress. 2019;35:e2882)

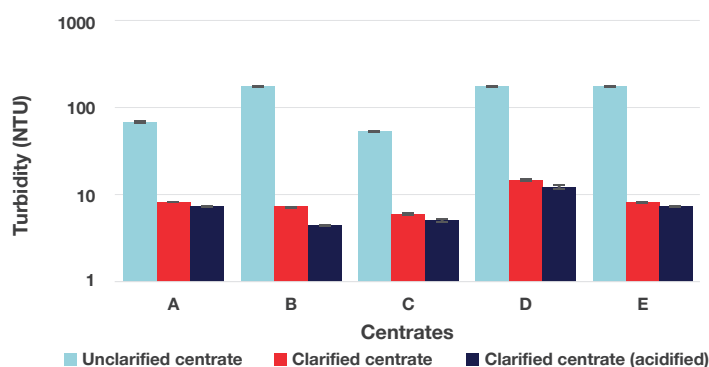


Figure 2: Turbidity Reduction by Thermo Scientific™ Harvest RC Centrate Chromatographic Clarifier. A - E are centrates from different CHO cell cultures.

Scalability

Harvest RC Centrate clarifier capsules scale linearly across laboratory, pilot, and manufacturing scale capsules. The fiber chromatographic clarification technology assures scalable performance from discovery to manufacturing scales. Performance is consistent from laboratory capsules (BC4 and BC25), scale-up capsules (BC170, BC340, and BC1020), to production capsules (BC2300 and BC18400) within ±20% of BC25 throughput.

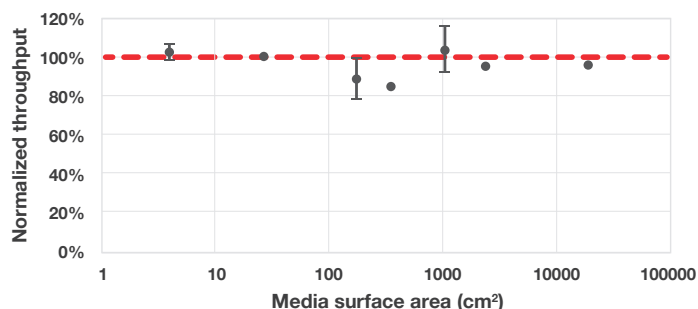


Figure 3: Scalability across Thermo Scientific™ Harvest RC Centrate Chromatographic Clarifier capsule sizes.

Performance data (continued)

Particle size control

Harvest RC Centrate clarifier provides effective reduction of a wide range of particle sizes that are typically present in centrate feed streams. The fiber chromatography technology is highly effective at capturing the population of <0.5 µm particles that are difficult to remove using traditional depth filtration.

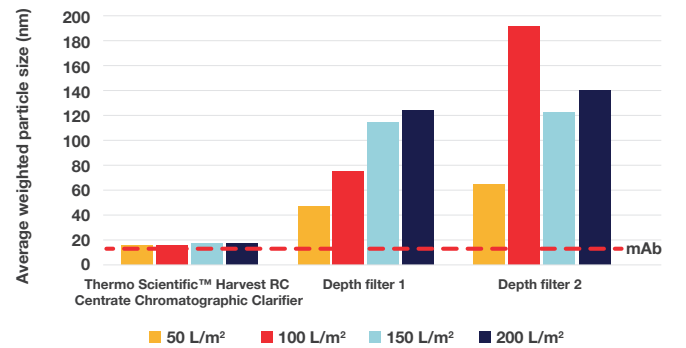


Figure 4: Average weighted particle size of clarified fluid by Thermo Scientific™ Harvest RC Centrate Chromatographic Clarifier capsules in comparison to cellulose-based depth filters.

Robust sterile membrane filter protection

Harvest RC Centrate clarifier enables efficient centrate clarification due to the highly effective chromatographic reduction of soluble and insoluble impurities. This allows effective protection of final sterilizing grade membrane filter down to 0.1 µm pore size.

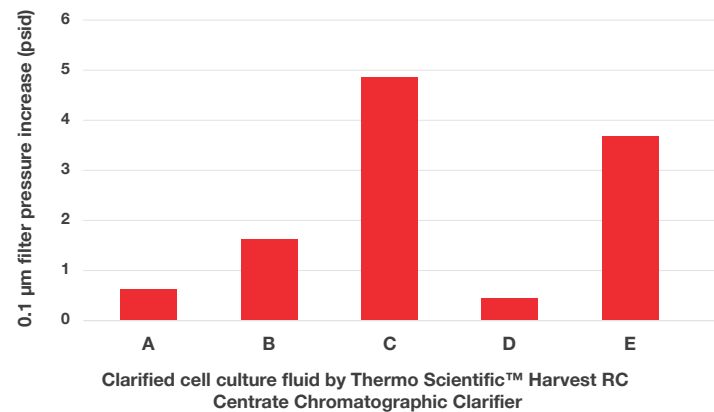


Figure 5: 0.1 µm sterile filter pressure increase at 500 L/m². A – E are clarified centrates from CHO cell cultures by Thermo Scientific™ Harvest RC Centrate Chromatographic Clarifier capsules.

Resisting clarification stage particle breakthrough

The Q-functionalized fibrous media and membrane of the Harvest RC Centrate clarifier can prevent particle breakthrough, which can impact membrane filter performance. With wet-laid media present in depth filters, particle breakthrough can occur creating pressure build up across the membrane filter stage which destabilizes the clarification process.

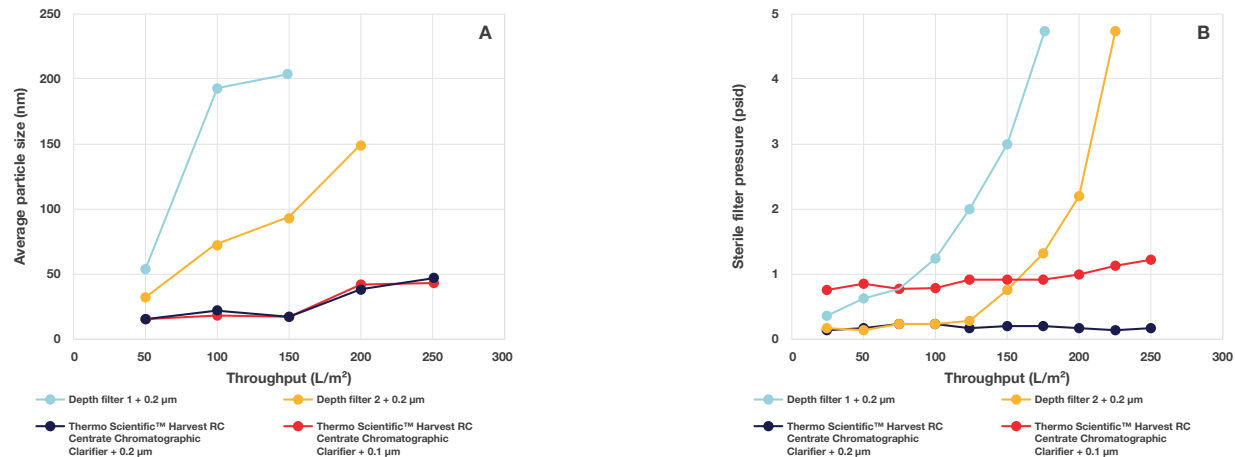
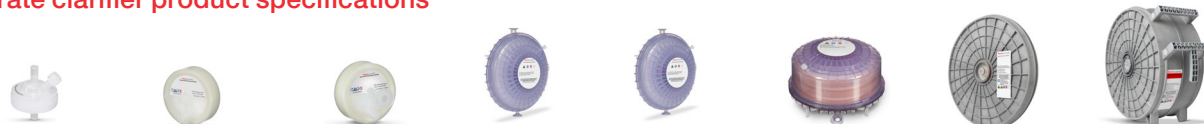


Figure 6: Prevention of particle breakthrough by Thermo Scientific™ Harvest RC Centrate Chromatographic Clarifier capsules, (A) average particle size of clarified fluid after 0.2 µm or 0.1 µm sterile filter, (B) sterile membrane filter pressure during centrate clarification. Each clarification train is challenged with CHO cell culture centrate.

Harvest RC Centrate clarifier product specifications



Product name	BC4	BC25 luer	BC sanitary	BC170	BC340	BC1020	BC2300	BC18400
Model name	EMP201RCC020R	EMP301RCC020R	EMP303RCC020R	EMP503RCC020R	EMP513RCC020R	EMP533RCC020R	EMP710RCC020R	EMP770RCC020R
Global part number	7100290386	7100290385	7100290387	7100326416	7100290384	7100290389	7100290388	7100290390
Secondary part number	70-0203-6505-5	70-0203-6506-3	70-0203-6507-1	70-0203-6660-8	70-0203-6508-9	70-0203-6509-7	70-0203-6510-5	70-0203-6511-3
Height x diameter	5.9 cm x 4.3 cm (2 5/16 in x 1 11/16 in)	4.5 cm x 7.7 cm (1 3/4 in x 3 in)	8.8 cm x 7.7 cm (3 5/16 in x 3 in)	10.1 cm x 24.1 cm (4 in x 9 1/2 in)	10.1 cm x 24.1 cm (4 in x 9 1/2 in)	15.2 cm x 24.1 cm (6 in x 9 1/2 in)	7.6 cm x 45 cm (3 in x 17 3/4 in)	22.2 cm x 45 cm (8 3/4 in x 17 3/4 in)
Dry weight	14.5 g	69.7 g	75.9 g	1.0 kg	1.1 kg	1.6 kg	3.6 kg	11.2 kg
Media surface area	3.8 cm ²	25 cm ²	25 cm ²	170 cm ²	340 cm ²	1020 cm ²	0.23 m ²	1.84 m ²
Centrate volume range (150-300 L/m ³) ¹	57 - 114 mL	375 - 750 mL	375 - 750 mL	2.55 - 5.1 L	5.1 - 10.2 L	15.3 - 30.6 L	34.5 - 69 L	276 - 552 L
Wet weight post blow down	16.8 g	82.2 g	88.7 g	1.2 kg	1.2 kg	2.2 kg	4.6 kg	19.2 kg
Fill volume ²	6.0 mL	27.5 mL	29.2 mL	0.74 L	0.64 L	1.60 L	3.8 L	16.2 L
Hold up volume post blow down ³	2.2 mL	12.4 mL	12.9 mL	0.14 L	0.18 L	0.53 L	1.0 L	8.0 L
Capsule material	Polypropylene	Polypropylene, glass filled polypropylene	Polypropylene, glass filled polypropylene	Polysulfone, polypropylene, thermoplastic elastomer, polypropylene, silicone	Polysulfone, glass filled polypropylene, thermoplastic elastomer, polypropylene, silicone	Polysulfone, glass filled polypropylene, thermoplastic elastomer, polypropylene, silicone	Polyphenylene oxide/polystyrene, polypropylene, glass filled polypropylene, thermoplastic elastomer, silicone	Polyphenylene oxide/polystyrene, polypropylene, glass filled polypropylene, thermoplastic elastomer, silicone
Inlet / outlet connections	Luer-Lok	Luer-Lok	¾-inch sanitary	¾-inch sanitary	¾-inch sanitary	¾-inch sanitary	1½-inch sanitary	1½-inch sanitary
Maximum inlet pressure ⁴	3.4 bar (50 psig)	2.8 bar (40 psig)	2.8 bar (40 psig)	3.1 bar (45 psig)	3.1 bar (45 psig)	3.1 bar (45 psig)	3.4 bar (50 psig)	3.4 bar (50 psig)
Maximum differential pressure	2.4 bar (35 psig)	2.4 bar (35 psig)	2.4 bar (35 psig)	2.4 bar (35 psid)	2.4 bar (35 psid)	2.4 bar (35 psid)	2.4 bar (35 psid)	2.4 bar (35 psid)
Maximum operating temperature	40°C (104°F)	40°C (104°F)	40°C (104°F)	40°C (104°F)	40°C (104°F)	40°C (104°F)	40°C (104°F)	40°C (104°F)
Required preconditioning rinse volume ⁵	9.5 mL	62.5 mL	62.5 mL	0.43 L	0.85 L	2.55 L	5.8 L	46.0 L
Required preconditioning rinse volume, post base sanitization ⁵	19 mL	125 mL	125 mL	1.70 L	3.4 L	10.20 L	23.0 L	92.0 L
Recommended use flow rate	0.63 mL/min	4.2 mL/min	4.2 mL/min	28 mL/min	57 mL/min	170 mL/min	0.38 L/min	3.07 L/min
Storage conditions	Controlled indoor temperature: 0 - 30°C (32 - 86°F) in original packaging	Controlled indoor temperature: 0 - 30°C (32 - 86°F) in original packaging	Controlled indoor temperature: 0 - 30°C (32 - 86°F) in original packaging	Controlled indoor temperature: 0 - 30°C (32 - 86°F) in original packaging	Controlled indoor temperature: 0 - 30°C (32 - 86°F) in original packaging	Controlled indoor temperature: 0 - 30°C (32 - 86°F) in original packaging	Controlled indoor temperature: 0 - 30°C (32 - 86°F) in original packaging	Controlled indoor temperature: 0 - 30°C (32 - 86°F) in original packaging
Shelf life	2 years from date of manufacture @ 30°C maximum storage temperature	2 years from date of manufacture @ 30°C maximum storage temperature	2 years from date of manufacture @ 30°C maximum storage temperature	2 years from date of manufacture @ 30°C maximum storage temperature	2 years from date of manufacture @ 30°C maximum storage temperature	2 years from date of manufacture @ 30°C maximum storage temperature	2 years from date of manufacture @ 30°C maximum storage temperature	2 years from date of manufacture @ 30°C maximum storage temperature
cGMP compliant	No	No	No	Yes	Yes	Yes	Yes	Yes
GLP compliant	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Please refer to the Thermo Scientific™ Harvest RC Chromatographic Clarifier product information sheet for product specifications and details of the Harvest RC clarifier.

Footnotes:

- Centrate volume range is the estimation for CHO cell culture centrates with acidified turbidity (acidified NTU) values of <1,000.
- Fill volume is defined as the volume of liquid that is required to fill the capsule.
- Post blow-down hold-up volume is defined as the volume of the residual liquid after air/gas blow down.
- Do not use this product for continuous service with compressed gasses. The use of compressed gas is permissible for post-use integrity testing and blow down purposes.
- A preconditioning rinse is required for the product to be compliant with USP Biological Reactivity Tests, including USP <87> and <88> Class VI. Refer to Installation and Operation Instructions for complete instructions on how to perform the preconditioning rinse.



Intended Use: Single-use filter 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, where applicable.

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

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