



Natrix® CH Membrane Chromatography Device

For single-use flow through aggregate removal

1. What are the benefits of membrane chromatography over resin/column chromatography?

Membrane chromatography has been developed to enable high levels of intensification in the downstream process. Chromatography membranes offer increased productivity by removing the reliance on diffusive mass transfer that characterizes resin process performance, enabling much reduced residence time requirements. In addition, membrane chromatography eliminates the in-between batch process burden (column cleaning, packing, re-validation) resulting in considerable time and cost savings.

2. How does cation exchange (CEX) chromatography work? What is CEX chromatography used for?

CEX chromatography is a purification technique based on electrostatic interactions. CEX ligands on beads or membranes are negatively charged, and therefore retain positively charged particles from the feed stream. In a monoclonal antibody (mAb) process, it is effective at separation of positively charged host cell proteins (HCPs) and aggregates from the mAb product.

3. What is frontal chromatography purification?

The CEX chromatography membrane is loaded under conditions that strongly bind the mAb product and then the aggregates displace the monomer product. As the media only binds impurities, it allows much higher loading, reduce the processing time resulting in increased productivity.

4. What is the typical mAb load capacity in frontal mode?

Natrix® CH devices can be loaded up to 1000 g/L in feeds with an aggregate content <4%. For feeds containing >5% aggregates, 400 to 800 g/L loading is typically achieved.

5. Can the device be used in bind and elute (B&E) mode?

Yes, the device works both in frontal and B&E modes.

6. Which chemistry (incl. ligands) are included in Natrix® CH devices? What functional groups are included in Natrix® CH devices/mixed-mode chemistry?

Natrix® CH devices contain a polyacrylamide hydrogel membrane that primarily consists of a sulfonic acid ligand with a low level of t-butyl functional groups.

7. How does Natrix® CH device differ from Eshmuno® CP-FT resin?

Eshmuno® CP-FT resin is a strong CEX resin designed for frontal chromatography mode, while Natrix® CH device contains a strong CEX membrane used in both B&E and frontal chromatography modes. Both products improve aggregate removal compared to standard resins. As Natrix® CH is a membrane-based solution, it enables very high flow rates. This results in increased productivity (×12) versus a standard resin. Its single-use (SU), plug-and-play (P&P), and miniaturized format enables flexibility with minimal changeover time between batches and reduced facility utilization.

8. When should I use Natrix® CH device and when should I use Eshmuno® CP-FT resin?

- Batch size, batches to purify per year, aggregate content, manufacturing set-up, and desire for process intensification/flexibility will all contribute to determining which product will work best. In general, we have seen comparable aggregate and HCP removal with better viral clearance for Natrix® CH devices compared to Eshmuno® CP-FT resin. For feeds with high levels of aggregates (>10%), Eshmuno® CP-FT resin usually works better.
- A head-to-head trial may be necessary to determine if there are molecule attributes which influence performance.
- A decision tool has been developed to define the best solution based on your needs. Please reach out to your local sales representative.

9. What is the pore size and bed height (depth) of Natrix® CH device?

The Natrix® CH device membrane thickness is 1.8 mm, and its pore size is approximately 1 µm. The device has 9 layers of membrane.

10. For which applications can Natrix® CH device be used?

Natrix® CH device is used for a wide range of biomolecules. Its primary application is monoclonal antibody/recombinant antibody polishing when used in frontal mode. It can also be used for viral applications and many applications that require a CEX chromatographic solution.

11. Is Natrix® CH applicable for commercial manufacturing activities?

Yes, the Natrix® CH device's maximum stackable volume of 3.7 L per holder combined with the device's unprecedented loading capacity (up to 1000 g/L) enables manufacturers to remove aggregates efficiently at all manufacturing scales depending on mAb titer and aggregate content.

12. How should I prepare the Natrix® CH device? Is there a need to sanitize and/or equilibrate Natrix® CH device prior to use?

Sanitization during priming with appropriate sanitants is recommended. The priming and equilibration procedure is described in the Natrix® CH device user guide. It is recommended that all buffers are filtered through 0.2 µm sterilizing grade or bioburden reduction filters such as Millipore Express® or Milligard® PES filters.

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13. How should I prepare the feed for its CEX polishing with Natrix® CH?

We recommend using Natrix® CH device post Protein A capture. Once the device is primed/equilibrated according to the procedure in the user guide, we recommend loading the feed at 10 MV/min. Please be aware that this flow rate is very fast compared to the membrane surface area and the hardware should be sized appropriately.

14. How many times can I reuse the device? How should I store it?

Natrix® CH device is a single-use device for each batch, hence reusing it for several batches is not recommended. By contrast, its cyclability without loss of performance has been demonstrated up to 20 cycles, feed dependent.

15. What are the recommended operating parameters (flow rate, pH and conductivity)? How can I maximize my end-product purity and my process yield using Natrix® CH device?

Generally, a 4–6 pH, 3–9 mS/cm conductivity and a 10 MV/min flowrate are recommended, but process development will enable the determination of the optimum conditions to maximize yield and impurity removal.

16. Can all Natrix® CH devices be manifolded together?

Pilot and process devices can be stacked together to reach up to 3.7 L membrane volume (10 process devices). They have the same number of membrane layers and relative hold-up volume to ensure scalability. If a higher total membrane volume is required, running 2 stacks in parallel (2 holders to reach a 7.4 L total membrane volume) is possible.

17. Can I use other holders (Pod, Viresolve® Pro, etc.)?

No, Natrix® devices have their own holders.

18. Can Natrix® CH device be used as part of a viral clearance strategy?

Yes. Natrix® CH device can contribute to the overall viral clearance strategy for downstream purification although the level of clearance will be dependent on operating conditions. A cumulative log removal value (LRV) of 3.3 for MVM (minute virus of mice) and 5.8 for XMuLV (xenotropic murine leukemia virus) has been demonstrated. Please refer to the datasheet for more information.

