Solutions for reduced carbon footprint and direct freshwater use in mAb manufacturing

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Reducing greenhouse gas (GHG) emissions

Sharp reductions in GHG emissions are needed to limit the global warming to 1.5°C above preindustrial global temperatures according to the Paris agreement. Estimates from the 2023 UN climate change conference (COP28) in Dubai call for a 43% reduction in GHG emissions by 2030 and 60% by 2035, relative to the 2019 level. Here we present ways to efficiently reduce GHG emissions in the protein A chromatography capture step for high demand monoclonal antibody (mAb) production.

Life cycle assessment (LCA)

LCA is a method to quantify the environmental impact of a product or a process. LCA data is fundamental for identifying hotspots, which are steps and inputs most responsible for negative environmental impact, and to make informed decisions during the optimization process. Here we are focusing on the impact category climate change which is the same as CO_2e or carbon footprint. We will also map the direct freshwater use in the protein A chromatography process. LCA data was generated according to ISO 14040-14044 standards and the methodology has been verified by a third party. SimaPro v9.5.0.0 software and the ecoinvent v3.9.1 database were used for background calculations.

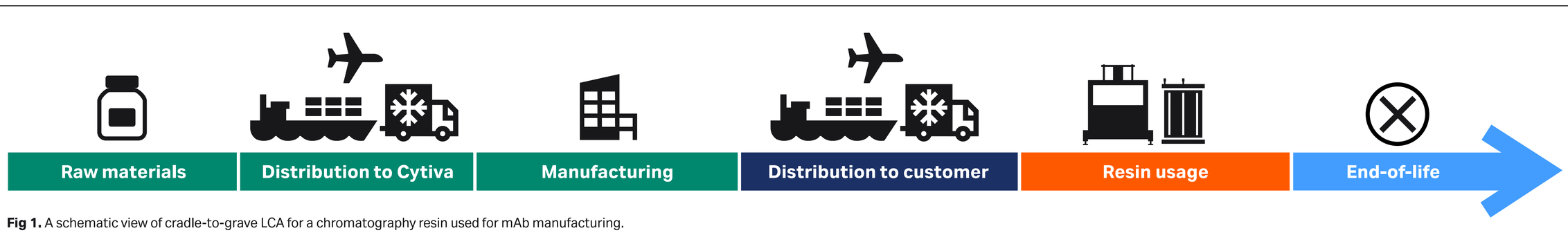


Fig 1. A schematic view of cradle-to-grave LCA for a chromatography resin used for mAb manufacturing.

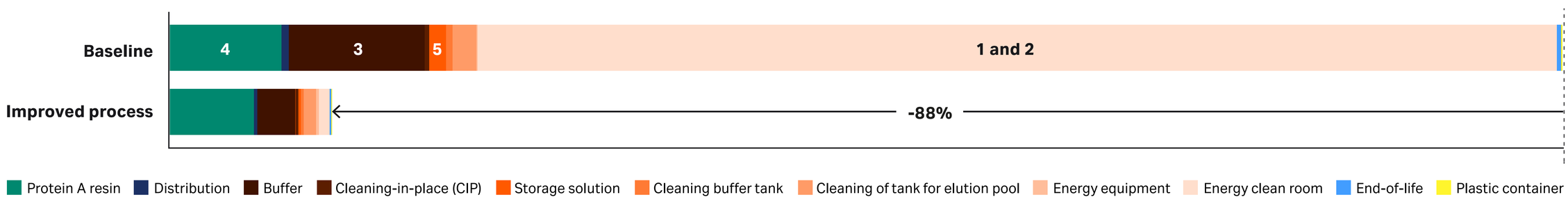
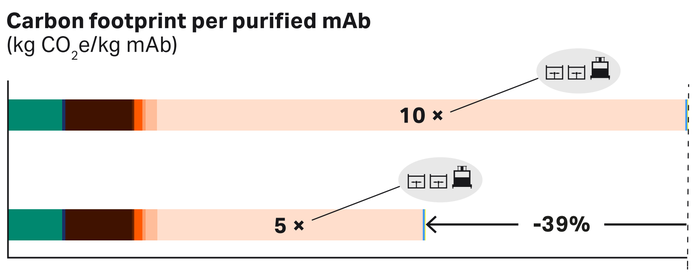


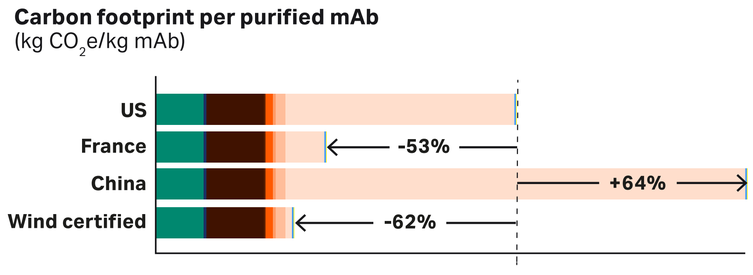
Fig 2. Carbon footprint split for baseline protein A chromatography process and the improved process. The numbers shown in the baseline process indicates the hotspots.

Hotspots and actions for reducing carbon footprint

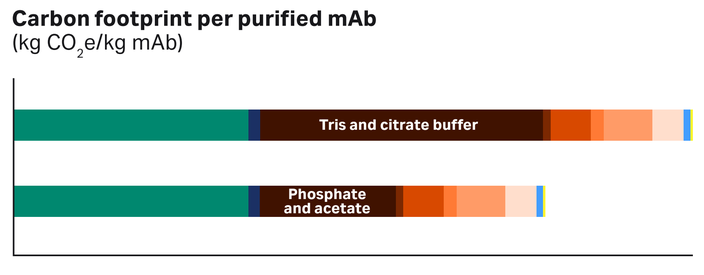
1. **Cleanroom size reduction.** The carbon footprint associated with the energy for operating the cleanroom infrastructure (heating, ventilation, and air conditioning [HVAC]) is the hotspot when using a US average electricity mix. The cleanroom area in the improved process was reduced from 10 to 5 × the equipment footprint.



2. **Switching to renewable energy source.** US average electricity grid mix was assigned as baseline reference. France represents predominantly nuclear power whereas China represents predominantly coal generated power. Wind-certified power represents a renewable electricity source resulting in 62% reduction of the carbon emissions in the improved process.



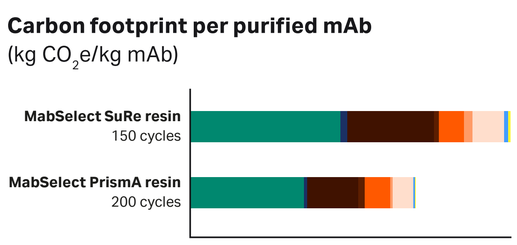
3. **Buffer system optimization.** The Cytiva platform buffers; phosphate and acetate, resulted in more than 50% reduction of the buffer related carbon footprint compared to the alternative buffer systems; tris and citrate.

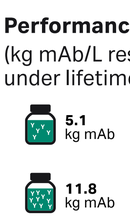


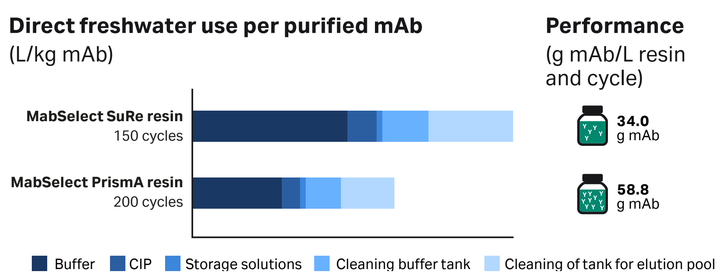
4a. **Reduced carbon footprint per kg mAb with MabSelect PrismA™ resin.** Excellent alkaline stability of MabSelect PrismA resin enables CIP with 0.5 M NaOH which prevents resin fouling and prolongs the resin lifetime compared to MabSelect SuRe™ resin. High mAb capacity and long resin lifetime increases the mass of mAb produced per L resin and lifetime.

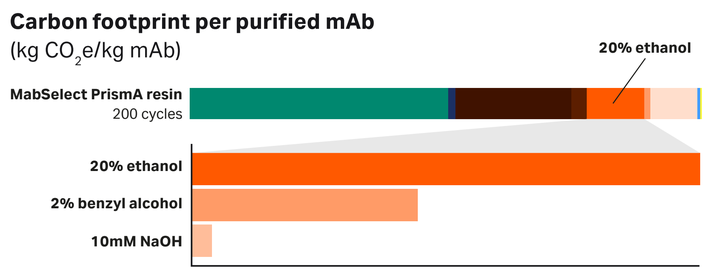
4b. **Reduced direct freshwater use with high-capacity MabSelect PrismA resin.** The buffer and CIP volumes per kg mAb is inversely proportional to the amount of mAb produced per L resin. The same relation is seen for the freshwater used for cleaning of the buffer and product pool tanks.

5. **Alternative column storage solutions.** 2% benzyl alcohol is lower carbon intense compared to 20% ethanol. 10 mM NaOH which has a very low carbon footprint can be used for short term storage of MabSelect PrismA columns between batches, provided the column wetted parts are compatible with NaOH.









Conclusions

- Decarbonization is urgent – the time is now.
- Measure and quantify for identification of hotspots.
- Impactful resource optimization enables up to ~ 90% carbon reduction of the protein A process.

Solutions for reducing environmental impact

- Process intensification for reduction of cleanroom size.
- Renewable energy source.
- Protein A chromatography resin with high-capacity and long resin lifetime.
- Buffer and storage solution optimization.

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