STATIC PERFORMANCE OF MABXPURE
APPLICATION NOTE #1

DAISEP MabXpure™, a disposable bead-based multimodal (SEC-AEX) flowthrough technology offering high depletion performances for Host Cell Proteins and DNA during clarification/harvest stages and sample preparation steps for mAb product solutions.

INTRODUCTION

Today, biopharmaceutical manufacturing has shown major improvements in upstream efficiency, with increasing titers (> 10 g/L) generally associated with high cell densities (> 60 x 10e6 cells/mL). Such increase in productivity is creating high levels of process-related impurities like greater HCP levels (> 800.000 ng/mL), host cell DNA (> 1000 ng/mL) content, HMW, fragments and/or lipids. This increase in bioburden and impurity levels shifts the production bottleneck to purification (clarification, chromatography and filtration). In this scenario, centrifugation and depth filtration techniques are reaching their limits, unable to provide a sustainable purification platform in terms of impurity reduction and/or bioburden depletion. DAISEP MabXpure has been developed to target these scenarios to ensure significant bioburden depletion with sustainable efficiencies of clarification. DAISEP MabXpure utilizes a combination of anion exchange (AEX) and size exclusion (SEC) mechanisms to trap the impurities whilst retaining mAbs in the flowthrough (Figure 1.). The bead design has been adapted to enable single-use flowthrough harvest operations using MabXpure as a filter aid in combination with depth filters (Figure 2.). DAISEP MabXpure can be mixed directly with the mAb feedstock to implement the bioburden depletion process. DAISEP MabXpure's high selectivity for impurities allows high HCP and DNA depletion (> 1 LRV) with high mAb recoveries (> 95%).

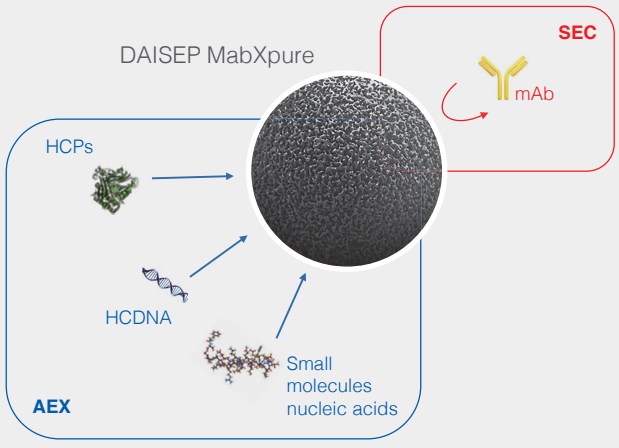

Figure 1. Multimodal depletion mechanisms of DAISEP MabXpure

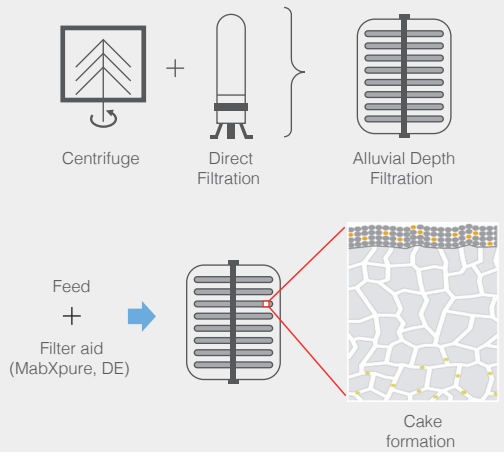

Figure 2. Cake / Alluvial filtration scheme

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MATERIALS AND METHODS:

LOAD MATERIAL
CHO-K1 clarified feed, spiked with mAb 2 g/L, HCP > 200 µg/mL, DNA > 1,000 ng/mL

BUFFER
Tris HCl 50 mM pH 7.4

DEVICE
MabXpure, DAISEP Spin centrifuge tubes

Depletion is performed by enabling product contact with the resin in different mix ratios i.e different ratios of DAISEP MabXpure with the CHO-K1 feed during 5 minutes contact time, and filtering off the resin with DAISEP Spin centrifuge tubes. Following this centrifugal filtration process, quantification of HCP is performed using the CHO-specific ELISA kits from Cygnus, DNA is quantified with Picogreen reagent and mAb titer is measured by HPLC-SEC. Additional contact times were utilized for 1:50 mix ratio.

RESULTS

In conventional clarification processes, where classic filter aids are used (silica or diatomaceous earth DE), either bioburden depletion is effective or there is an effective mAb recovery obtained (Figure 3.). There is always a trade-off on recovery or bioburden depletion depending on which one takes precedence. However, with DAISEP MabXpure there is combined efficacy in terms of bioburden removal (> 1 LRV) and antibody recovery (> 80%). These performances are guaranteed and observed even when DAISEP MabXpure is diluted up to 1:20 mix ratio, representing ideal conditions for sample preparation and harvest process operations (Figure 3.). If necessary, the depletion performances can be increased with higher contact times (Figure 4.) inducing lower residual HCP and by reaching 2 LRV of DNA.

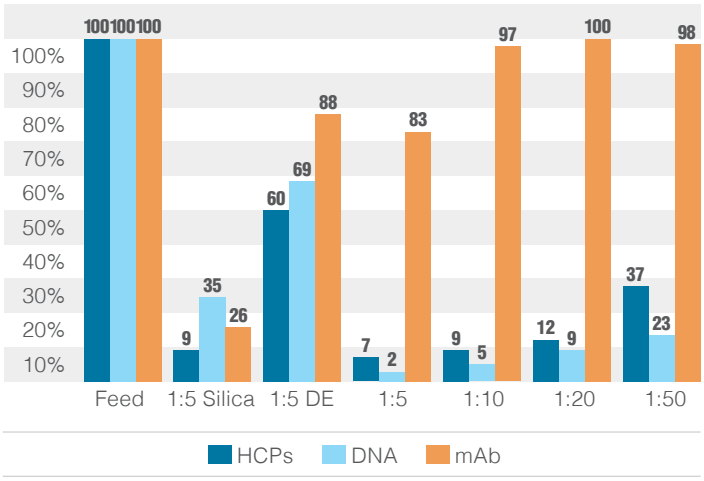

Figure 3. Residual HCP, DNA and mAb recovery with different mix ratios of DAISEP MabXpure

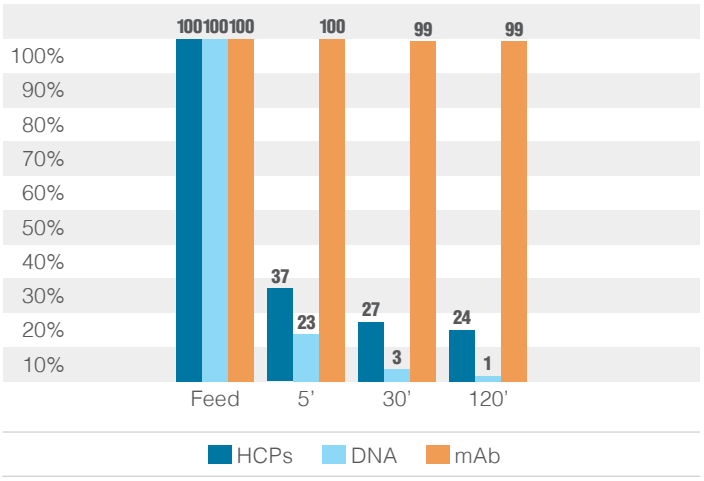

Figure 4. Impact of contact time on residual HCP, DNA and mAb recovery (1:50 mix ratio)

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DISCUSSION:

The use of MabXpure in static mode fits naturally in a process where depth filters are used since the resin is eliminated by cake filtration or alluvial depth filtration. As a consequence, the number of depth filter sheets is adapted to the amount of filter aid to be removed.

DAISEP MabXpure can also be combined with diatomaceous earth with unclarified feedstocks achieving good turbidity clearance < 10 NTU starting with feeds > 4000 NTU. Ideally, DAISEP MabXpure's conditions of use are optimal with high mix ratios and short contact times for sample preparation, or lower mix ratios and higher contact times for in-process applications. The flexibility of utilising the resin in the process, in this manner, enhances its single-use and flowthrough quality attributes enabling the ease of implementation of MabXpure in the process.

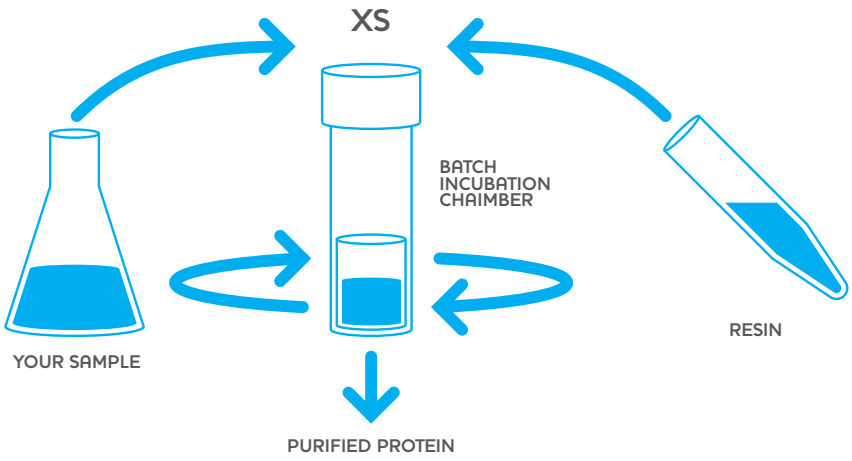
CONCLUSION

DAISEP MabXpure has a very high capability for depleting host cell proteins and DNA, with extremely high mAb recovery.

Depending on the process conditions, the capacity of DAISEP MabXpure helps to remove up to 1 LRV of HCP and 2 LRV of DNA in one static mode step.

The unique flexibility of DAISEP MabXpure allows the user to choose the mode of action with an optimal mix ratio and contact time to make the resin an ideal filter aid for clarification/harvest steps by cake or alluvial filtration.

DAISEP MabXpure can be implemented from lab scale to process scale with DAISEP Spin columns to depth filter sheets respectively.



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DAISEP MABXPURE RANGE

MABXPURE BULK	
MabXpure bulk 50 mL	DMXBK0050
MabXpure bulk 500 mL	DMXBK0500
MabXpure bulk 1000 mL	DMXBK1000
MabXpure bulk 10L	DMXBK10

50 mL 500 mL

MABXPURE FT	
MabXpure FT 1 mL (5 units/pack)	DMXFT0001
MabXpure FT 5 mL (5 units/pack)	DMXFT0005
MabXpure FT 50 mL (1 unit)	DMXFT0050
MabXpure FT 500 mL (1 unit)	DMXFT0500
MabXpure FT 1.5 L (1 unit)	DMXFT1500

1 mL 5 mL

MABXPURE KIT	
MabXpure Kit	DMXKT0001

MABXPURE KIT

DAISEP SPIN XS & XL	
DAISEP Spin XS (40 units/pack)	DSPXS0040
DAISEP Spin XL (8 units/pack)	DSPXL0008


XS XL

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