



## MabXpure for Innovative HCP Clearance Strategies and Flowthrough platform enabling technologies

Fabien Rousset, Ph.D., DAICEL Bioseparations, Chiral Technologies Europe, France



Mathieu Porte, Senior Scientist Bioproduction, PolyPlus Transfection, France

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*Thursday 12th Sept, 2019*



13.000 employees , >\$4B revenues (2018)

1919	Dainippon Celluloid Company
1934	Creation of Fujifilm
1966	Daicel Corporation
1970	Daicel-Evonik
1988	Daicel-UCB
1990	Chiral Technologies (Pharma)
2016	Daicel Bioseparations (Biopharma)
2018	Daicel Life Sciences



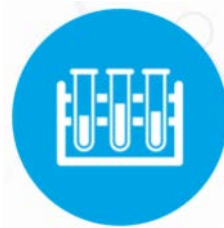
Reagents



Pharma Services



Standards



Excipients



Chromatography



Bioseparations



Genomics

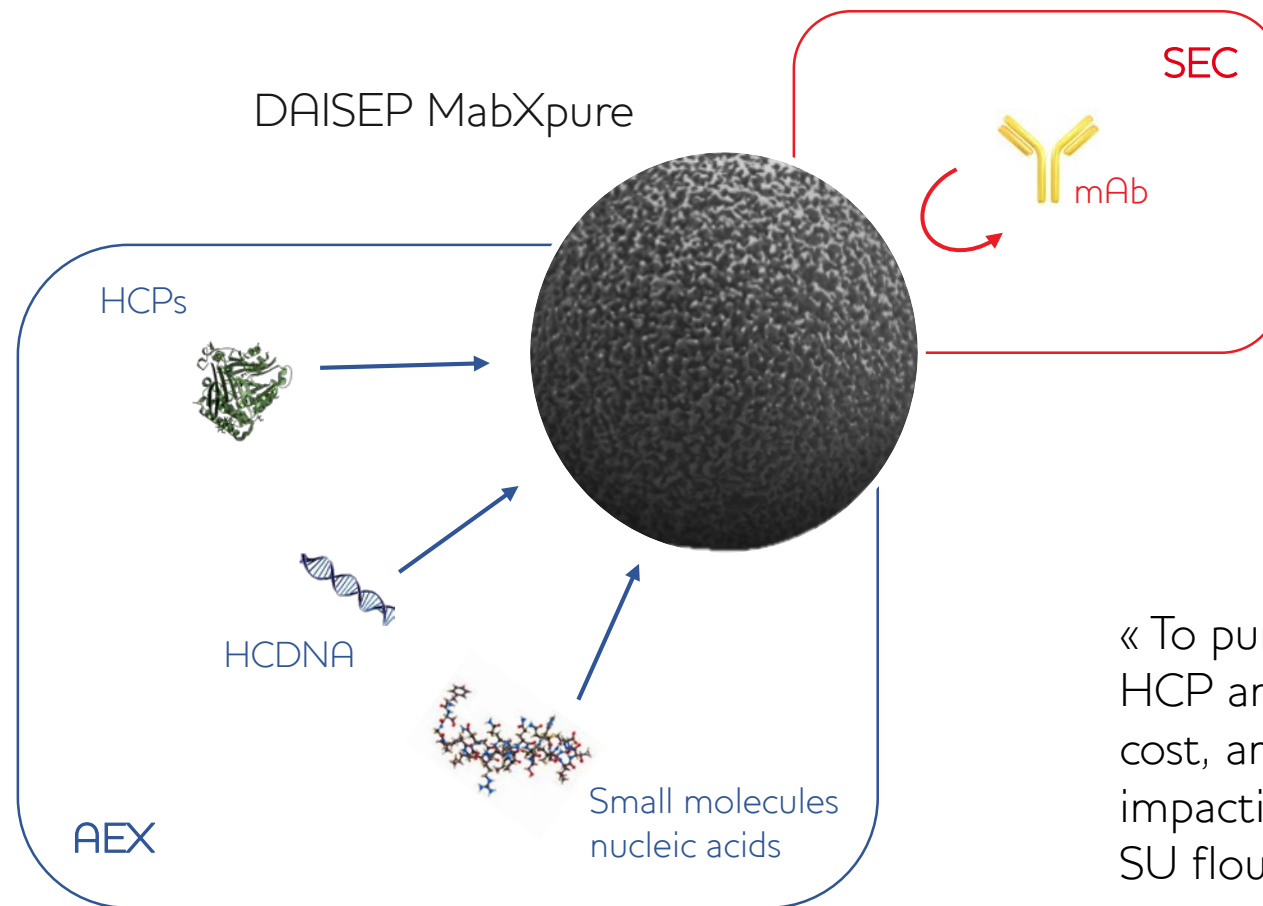


Intracell. Delivery



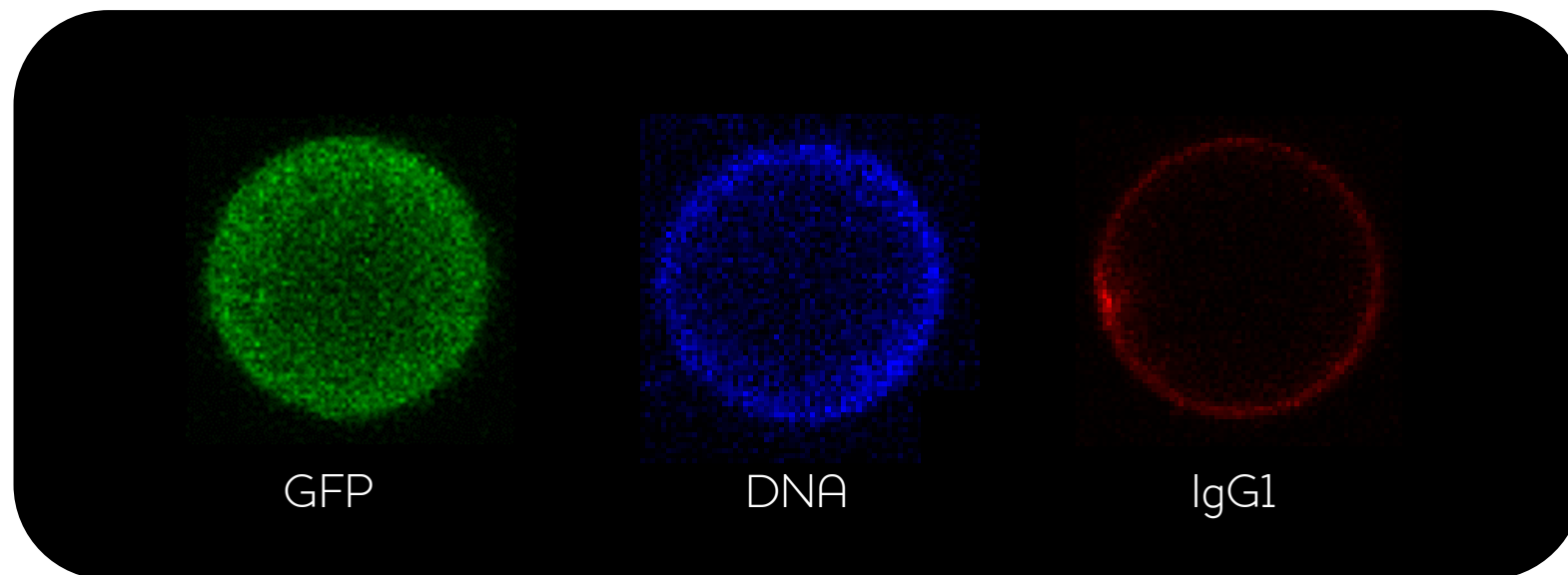
## Outline

- 1 DAISEP MabXpure introduction
- CS Case Study with Polyplus Transfection
- 2 Additional features
- 3 DAISEP MabXpure range



« To purify large quantities of HCP and bioburden, at low cost, and quickly, without impacting mAb recovery, in a SU flowthrough method »

## Confocal Fluorescence Microscopy – SEC/AEX



HCP  
27kDa pI 5.8  
AEX



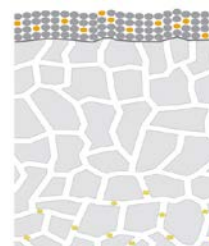
DNA  
100-300kDa pI 5.5  
AEX-SEC



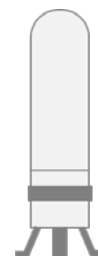
IgG  
150kDa pI 8.3  
SEC

# Flexibility is key

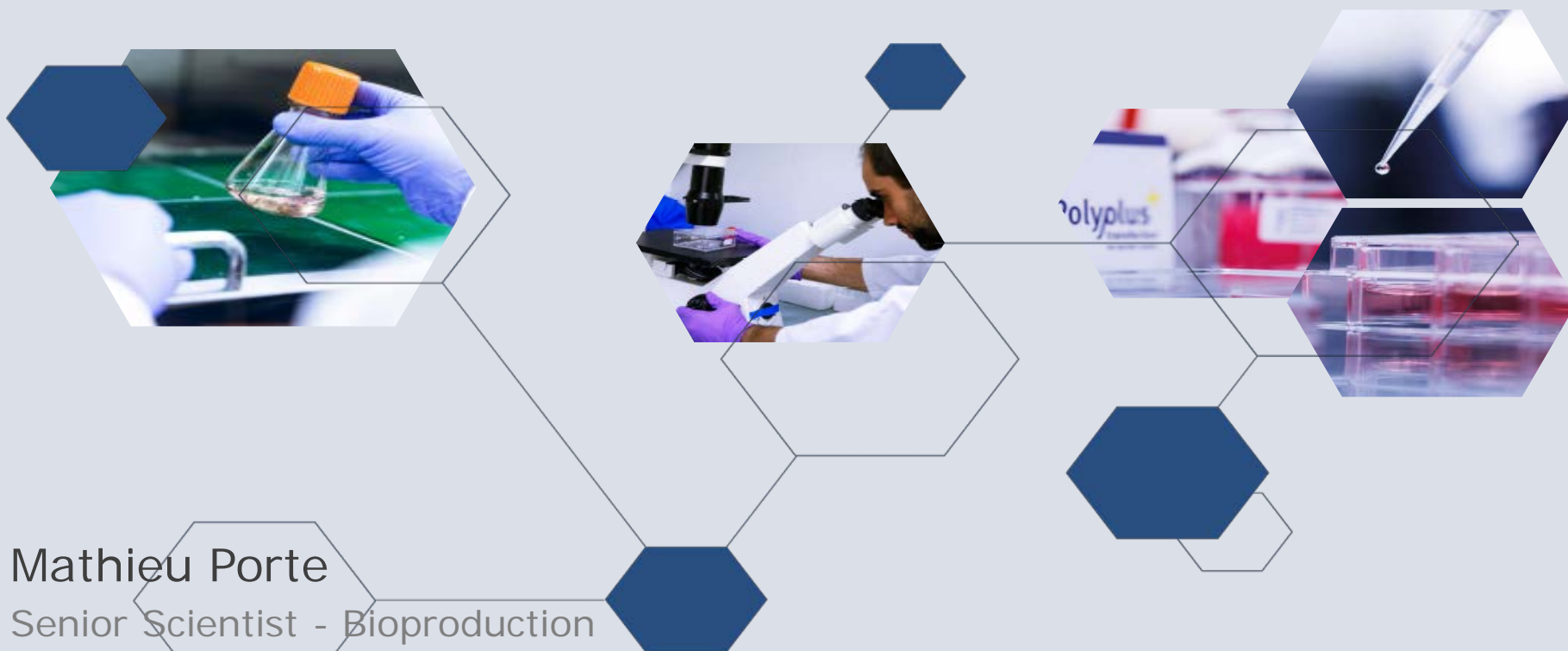
DAISEP MabXpure as a filter aid



DAISEP MabXpure FT as a cartridge



# MabXpure Evaluation



Mathieu Porte

Senior Scientist - Bioproduction

Jonathan Havard

R&D research assistant - Bioproduction



## Innovative transfection solutions to accelerate your research



- ✦ Wide range of products for research, process development, bioproduction and *in vivo* applications
- ✦ 18 years of expertise in transfection at your service
- ✦ GMP grade reagents available
- ✦ Tailored scientific, technical and regulatory support
- ✦ High quality reagents made in France



## + Transfection Solutions for R&D

- + Academic and University research laboratories, research department of biotechs and pharmas
- + Labs performing day-to-day transfection experiments



## + Transfection Solutions for Direct Therapy

- + Reagents for direct administration to human
- + The reagent delivers the active drug

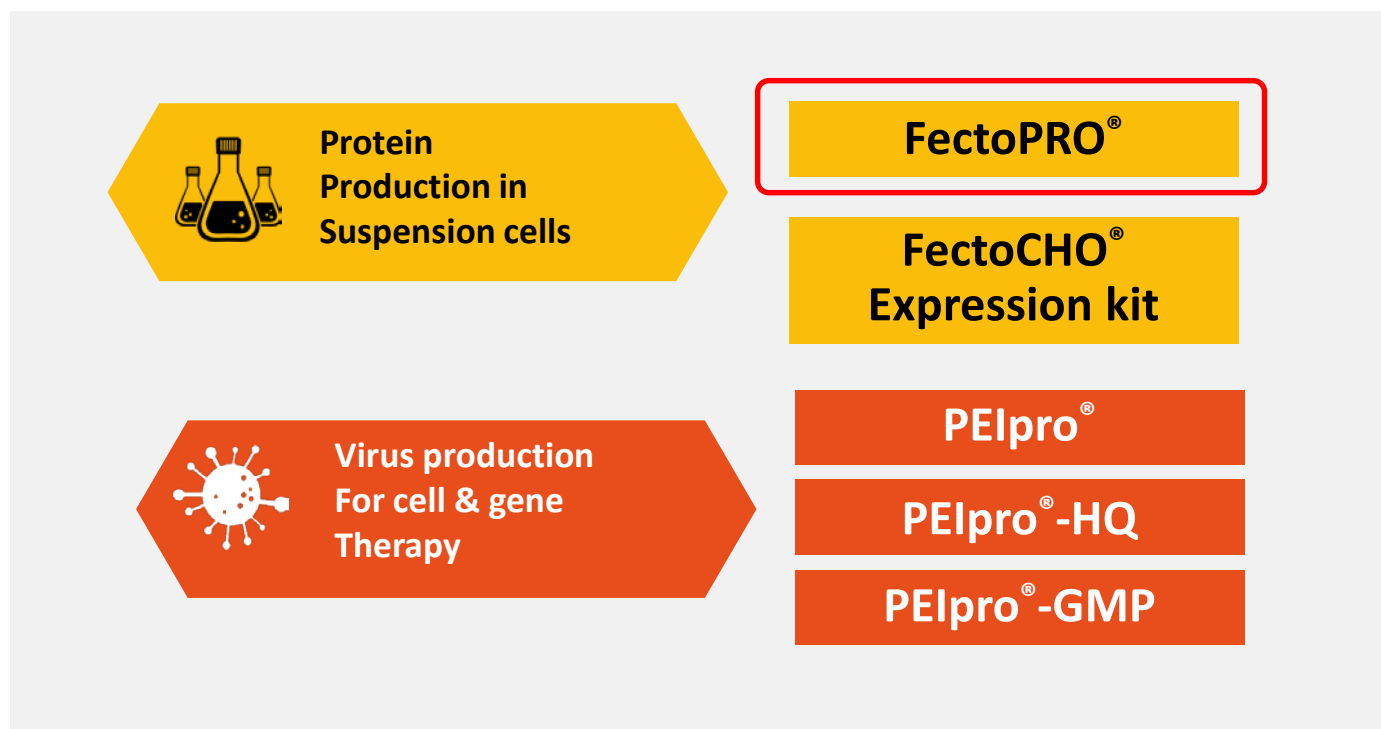


## + Transfection Solutions for Production of Biologics

- + Reagents for use in industrial process
- + To produce biotherapeutics at large scale (virus or protein)

# Bioproduction Product Portfolio

①  
C  
②  
③



# Stable vs Transient Protein Production

1  
C  
2  
3

## + Stable clone establishment



High quality proteins, very high yields



Complex process, time consuming

## + Transient Expression



High quality proteins, fast and flexible process



Limited protein yield

## ✦ Transient antibody production:

- ✦ High number of samples
- ✦ Production of various antibodies (screening)
- ✦ Small to mid-scale production

## ✦ Problematic:

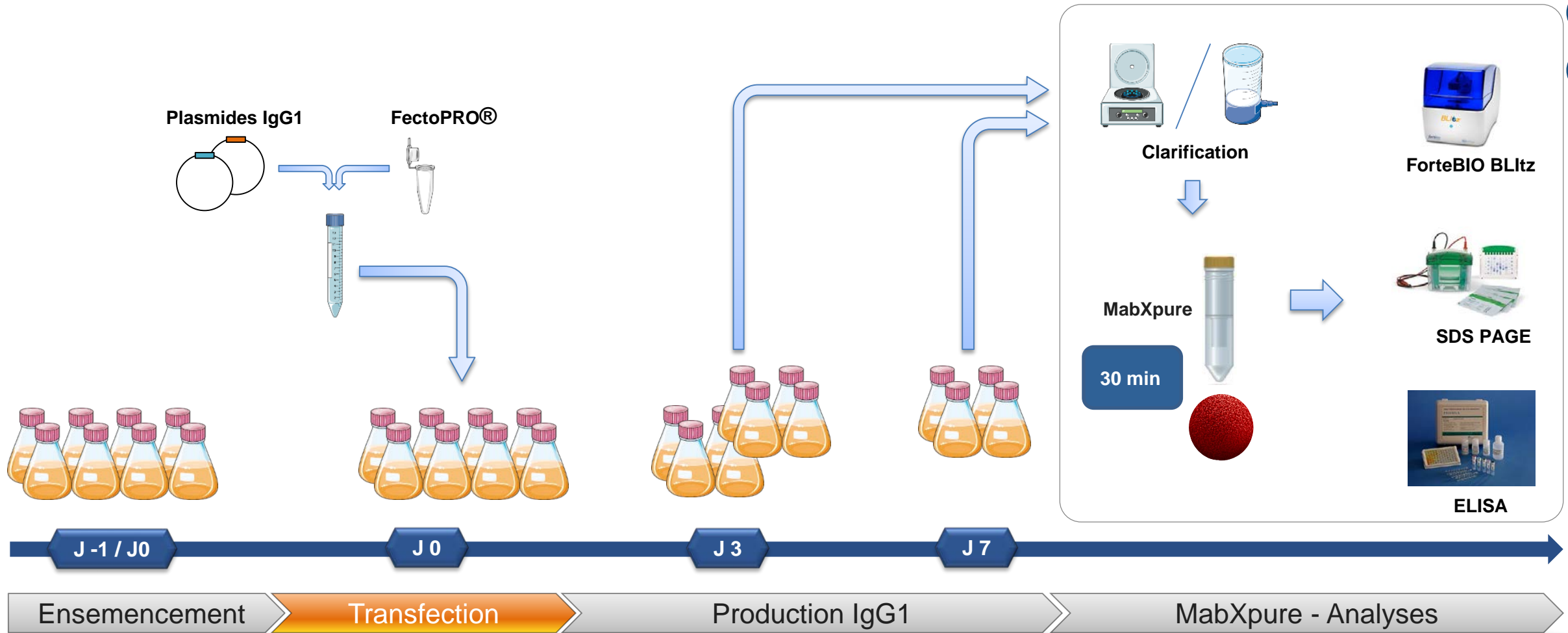
- ✦ Antibodies have to be pre-purified in order to assess their biological activity
- ✦ Host cell protein and DNA are difficult to remove contaminants and can reach up to 400.000 ng/ml and 20.000 ng/ml respectively

## ✦ Needs:

- ✦ Efficient depletion of HCPs and DNA
- ✦ Fast and flexible method
- ✦ Not dependent on the protein to be purified

# Seeding – Transfection – Cell Growth - Analyses

①  
C  
②  
③

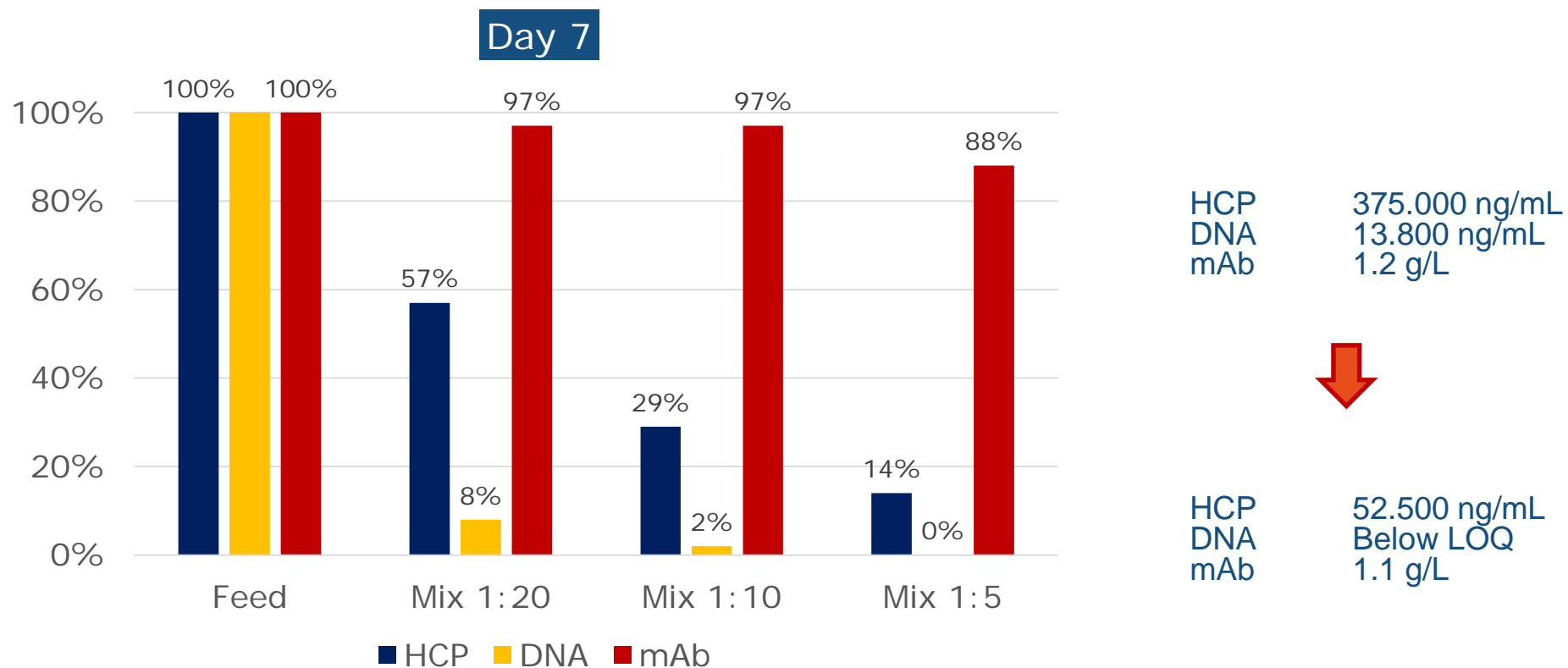


# Expi293



# Expi293 – Residual HCP&DNA / IgG1 Recovery

①  
C  
②  
③



# Expi293 – SDS PAGE

Day 3



- Bio-rad Criterion system
- Gel TGX 4-15%
- Tampon Tris/Gly 0,1% SDS
- Sample buffer Native All Blue + 2% SDS
- Dilution 1/2 des échantillons
- Migration 30' à 200V
- Coloration Bleu Coomassie

Ladder  
Centrifugation  
Mix ratio 1:10  
Mix ratio 1:20  
Centri + Filtr.  
Mix ratio 1:10  
Mix ratio 1:20

L

C

M1

M2

CF

M1

M2

L

C

M1

M2

CF

M1

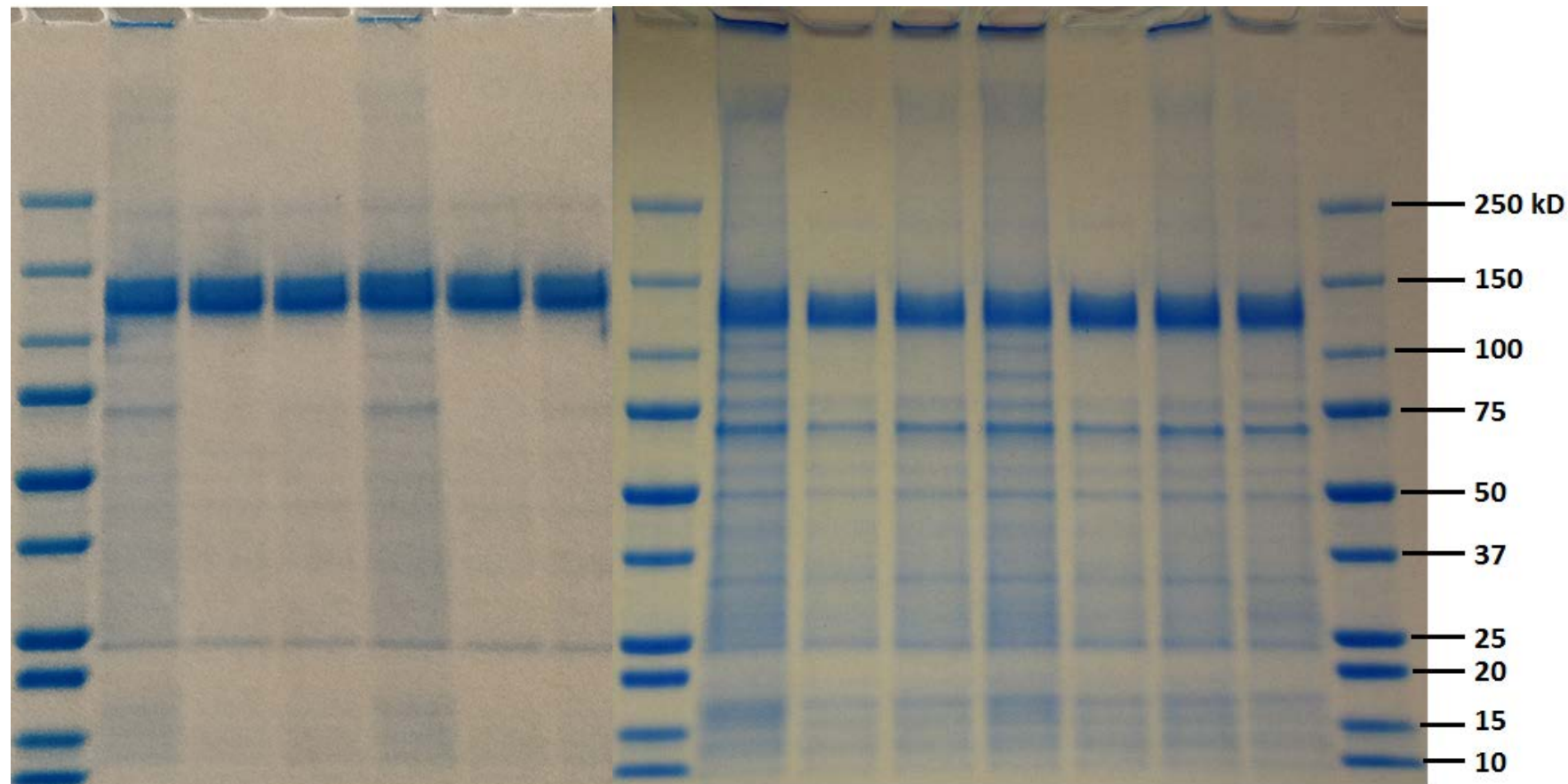
M2

S

L

Sartoclear

Day 7



①  
C  
②  
③

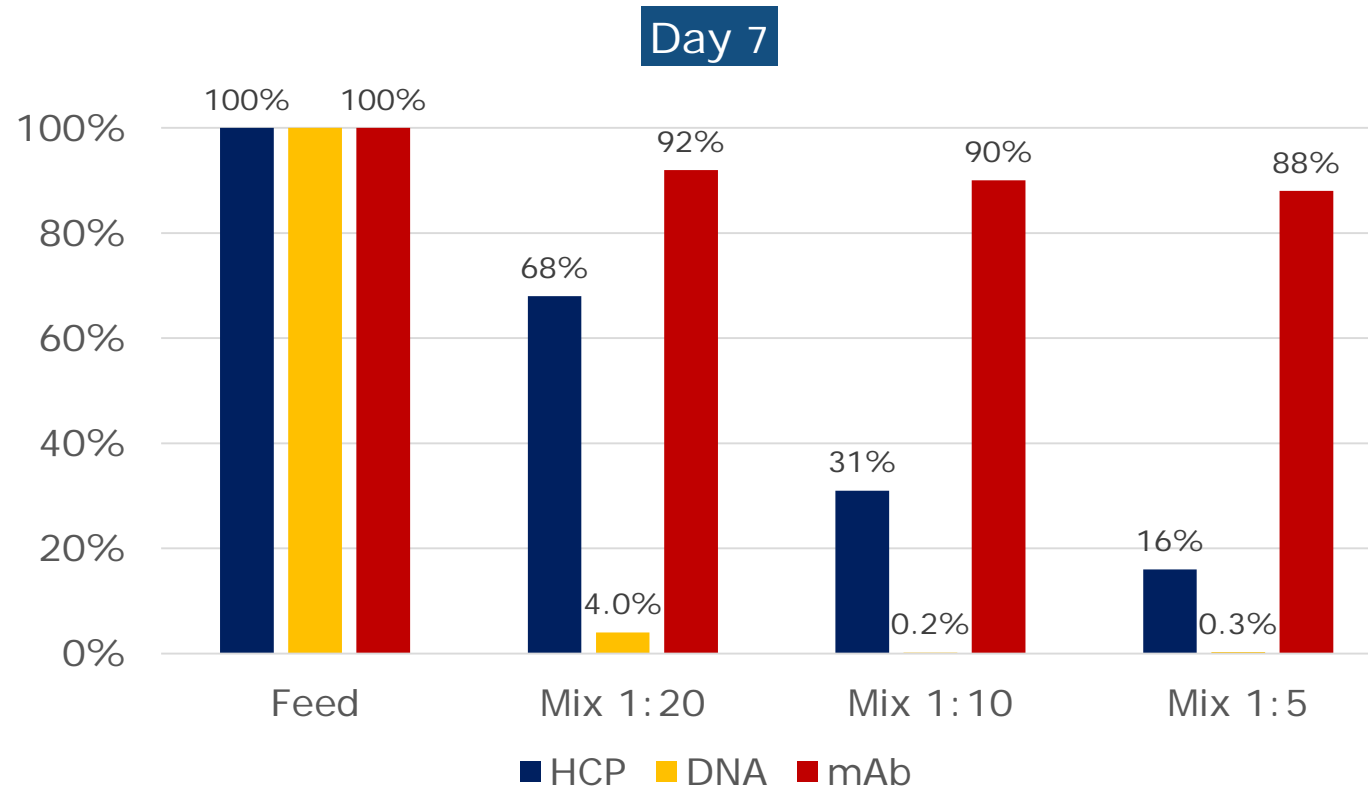
# ExpiCHO-S

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# ExpiCHO-S - Residual HCP&DNA / IgG1 Recovery

①  
C  
②  
③



HCP 414.000 ng/mL  
DNA 15.900 ng/mL  
mAb 0.65 g/L



HCP 64.900 ng/mL  
DNA 31 ng/mL  
mAb 0.6 g/L

# ExpiCHO-S – SDS PAGE

①  
C  
②  
③

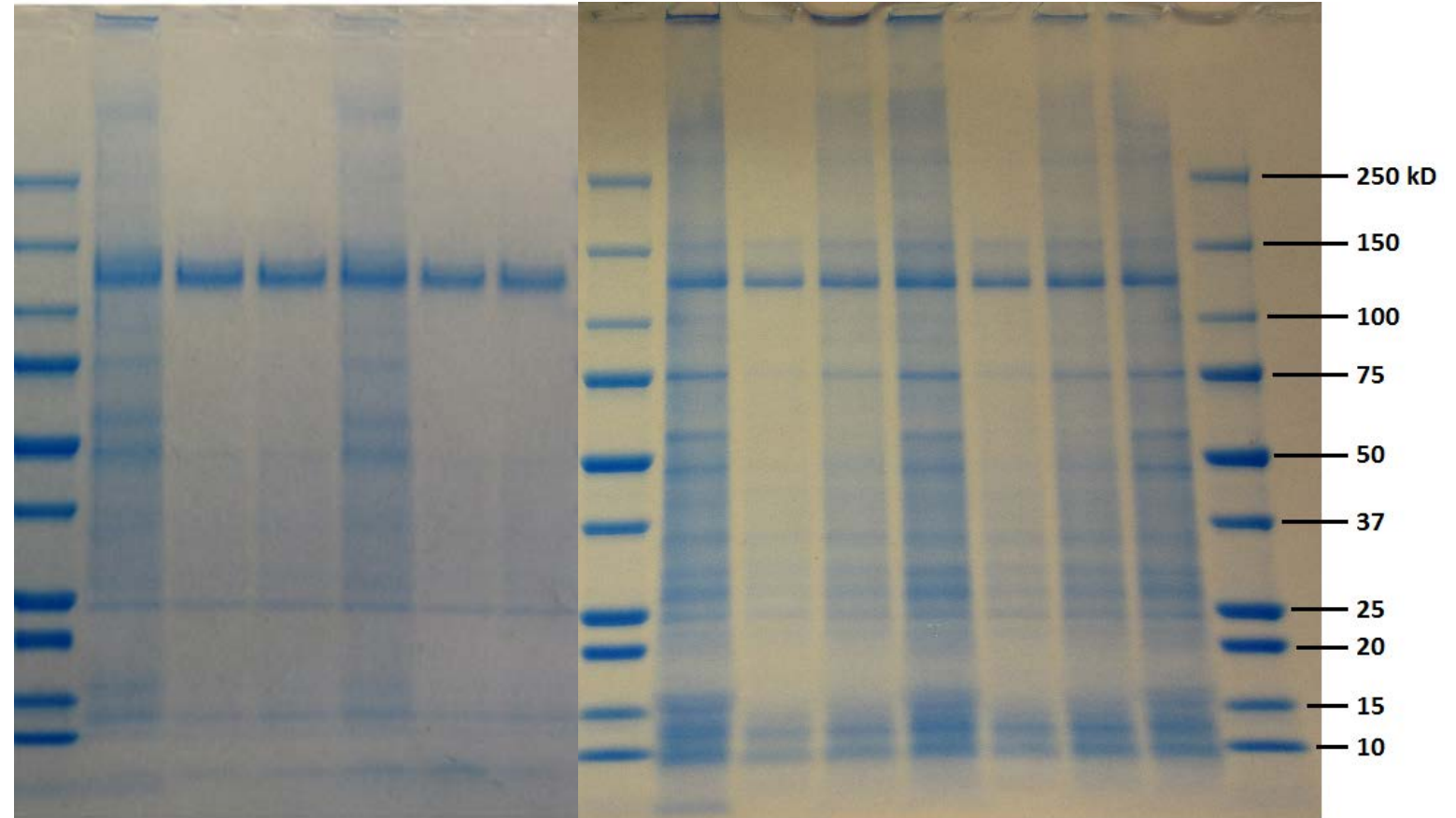
Day 3



- Bio-rad Criterion system
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- Sample buffer Native All Blue + 2% SDS
- Dilution 1/2 des échantillons
- Migration 30' à 200V
- Coloration Bleu Coomassie

Ladder Centrifugation Mix ratio 1:10 Mix ratio 1:20 Centri + Filtr Mix ratio 1:10 Mix ratio 1:20 Sartoclear

L C M1 M2 CF M1 M2 L C M1 M2 CF M1 M2 S L



Day 7

## ✦ MabXpure Evaluation:

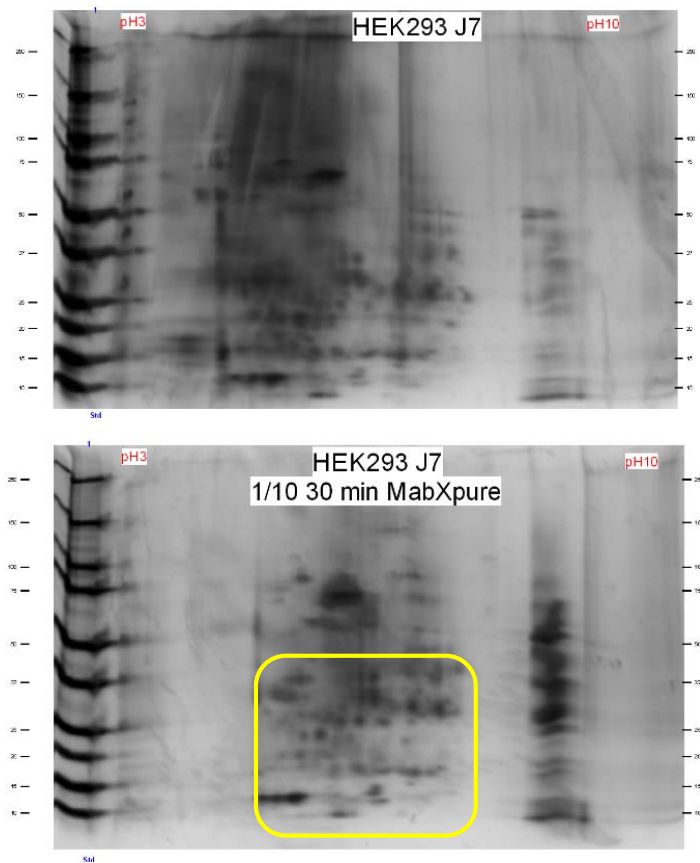
- ✦ High HCP and DNA depletion after Day 7 (higher for Day 3)
- ✦ Excellent mAb recovery for Expi-CHO S and Expi-293 (from 88 to 97%)
- ✦ Easy to use at lab scale

## ✦ Features:

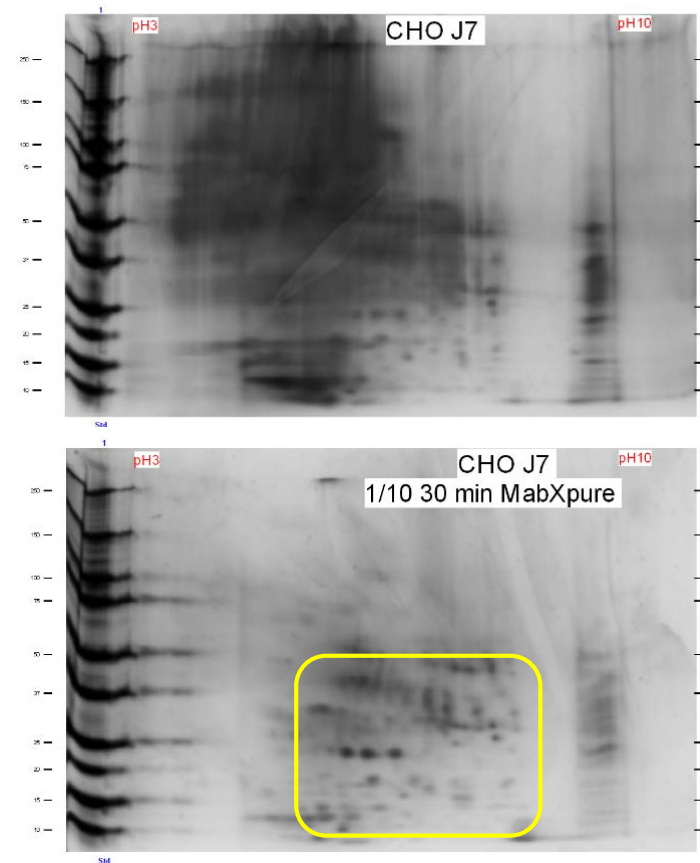
- ✦ Clear depletion observed with SDS-PAGE gel
- ✦ Fast and flexible method to get purified mAb (time, mix ratio...)
- ✦ Up to 1LRV for HCP with 1:5 mix ratio
- ✦ >2 LRV for DNA with 1:5 mix ratio

➡ DAICEL MabXpure offers an easy and flowthrough pre-purification solution

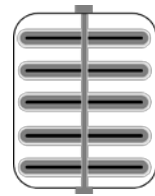
Expi 293



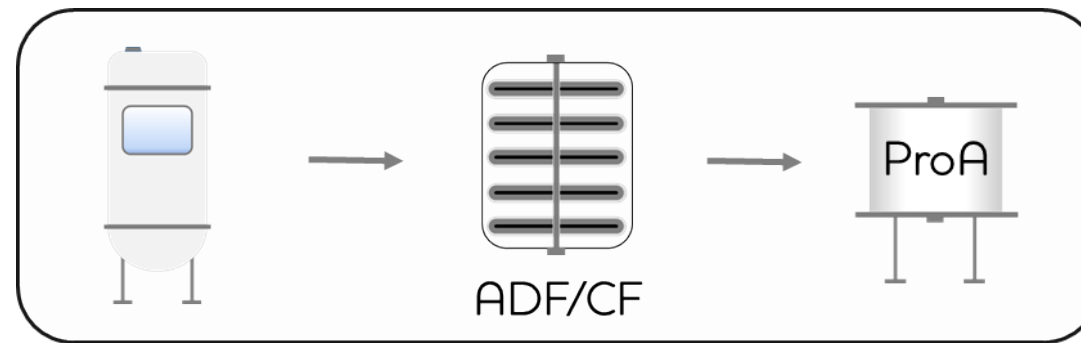
ExpiCHO-S



## Optimized Clarification Platform « MabXpure + »



Cellulose-based depth filter sheet  
Immobilized activated carbon  
Mesopores \*



### Feed 1:

- HCP: 800.000 ng/ml
- HMW: 6%

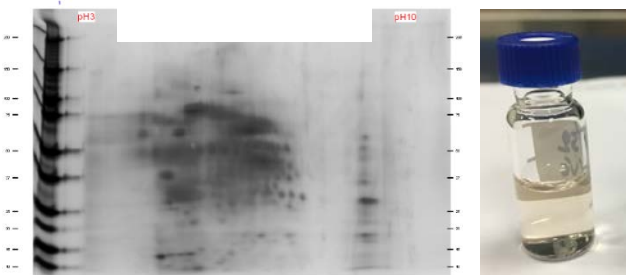
### Feed 2:

- HCP: 200.000 ng/mL
- HMW: 8.8%

### Post ProA resin

- HCP: 200 ng/ml (<50 ppm)
- HMW: 0.5%

DS criteria are obtained after proA  
Using « MabXpure + » platform

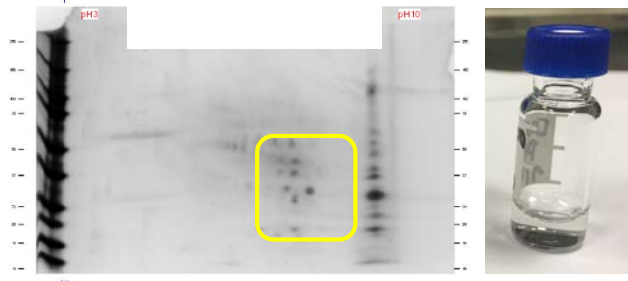


### Feed 1:

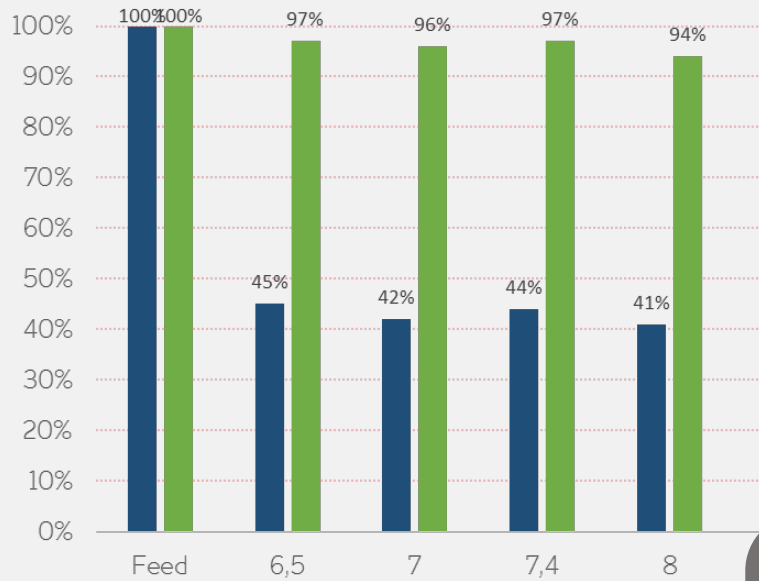
- HCP: 17000 ng/ml (98% depletion)
- HMW: 0.6%

### Feed 2:

- HCP: <1.600ng/mL (>99% depletion)
- HMW: 1%

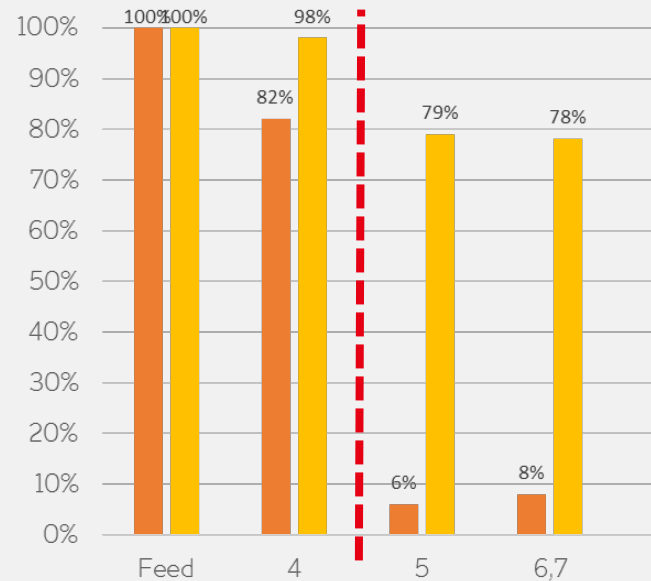


pH of Feed



■ HCPs ■ IgG

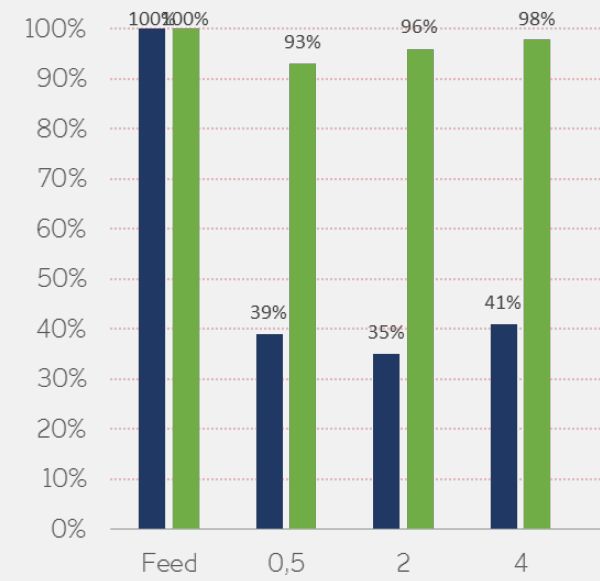
pH vs pI



■ OVA ■ bIgG

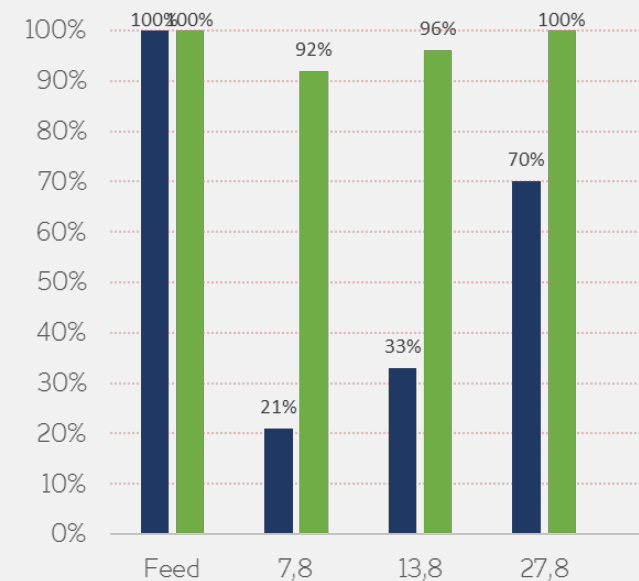
CHO-K1  
DNA 1.000 ng/mL  
HCP 180 µg/mL  
IgG 2 mg/mL

pI<sub>OVA</sub> 4.5  
pI<sub>bIgG</sub> 5.4-8.5



■ HCPs ■ IgG

Titer g/L



■ HCPs ■ IgG

Conductivity

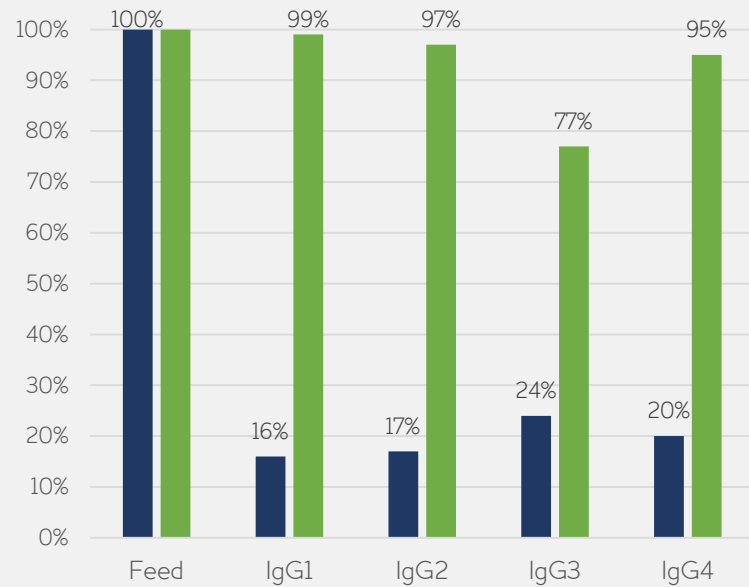
1

C

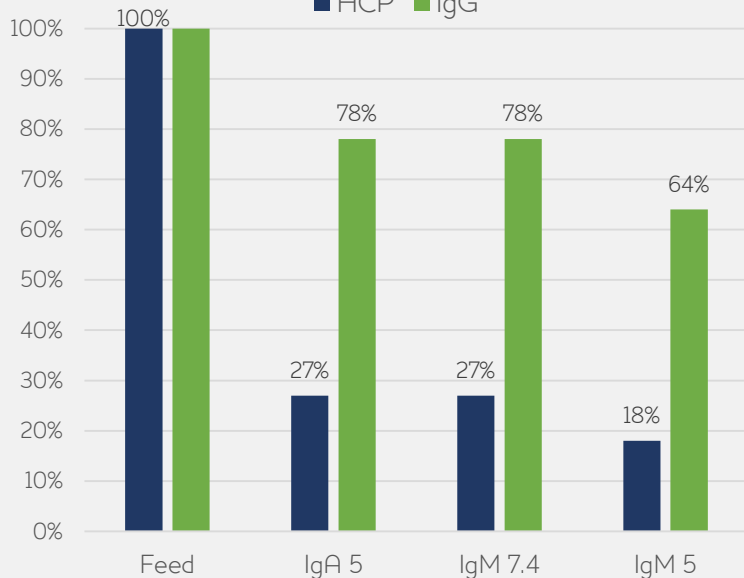
2

3

## IgG subclasses



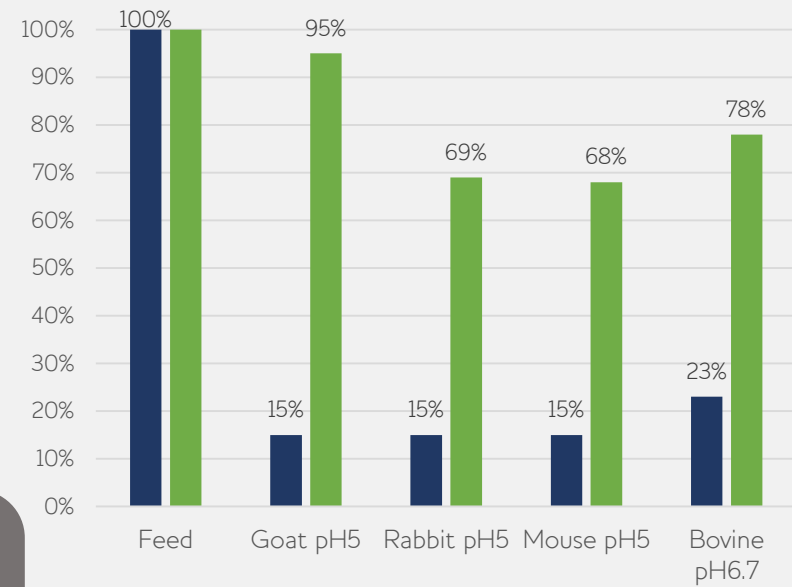
■ HCP ■ IgG



■ HCP ■ IgG

## IgG types

Mix ratio 1:20  
DNA 500 ng/mL  
HCP 70 µg/mL  
IgG 2 mg/mL

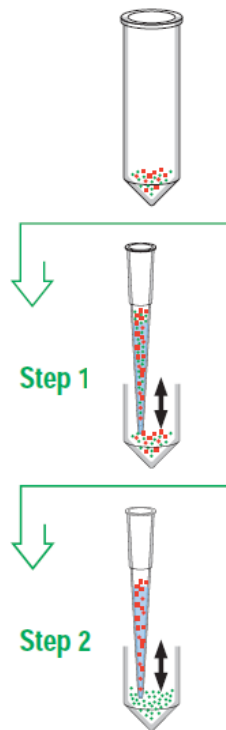


■ HCP ■ IgG

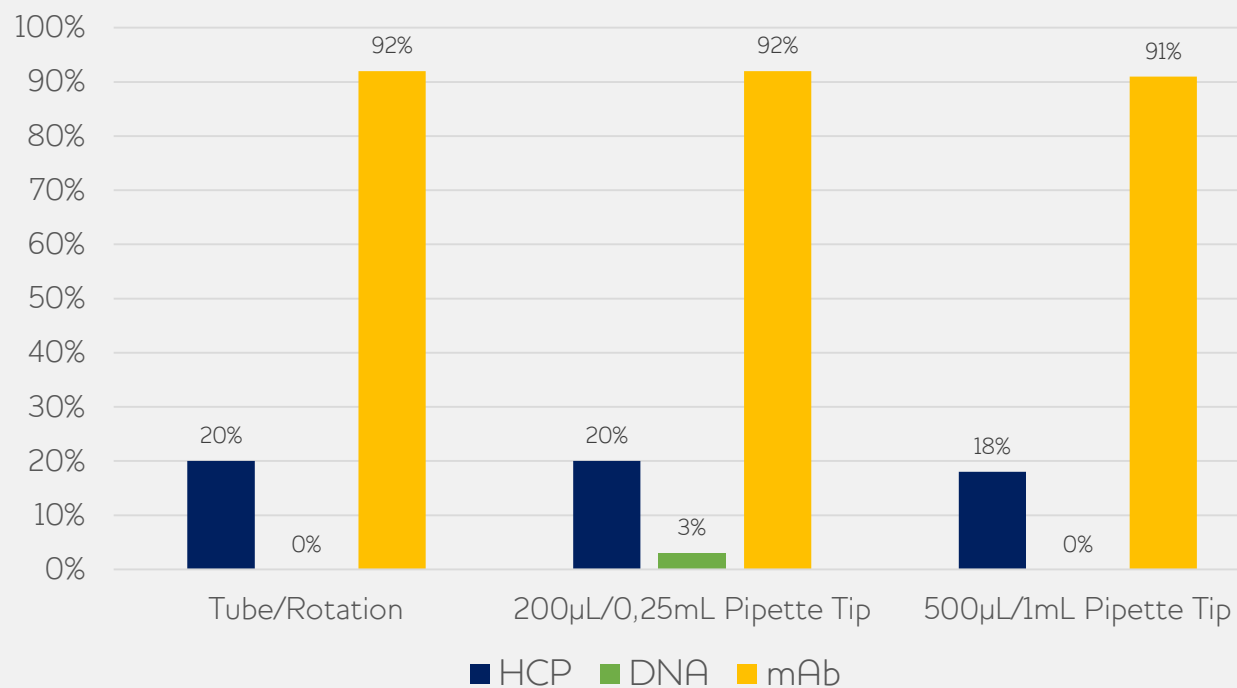
## IgG Origins

MabXpure is working for all:

- IgGs subclasses
- IgGs origins
- IgM & IgA



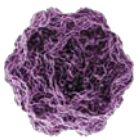
## Depletion and Recovery when MabXpure In Pipette Tip



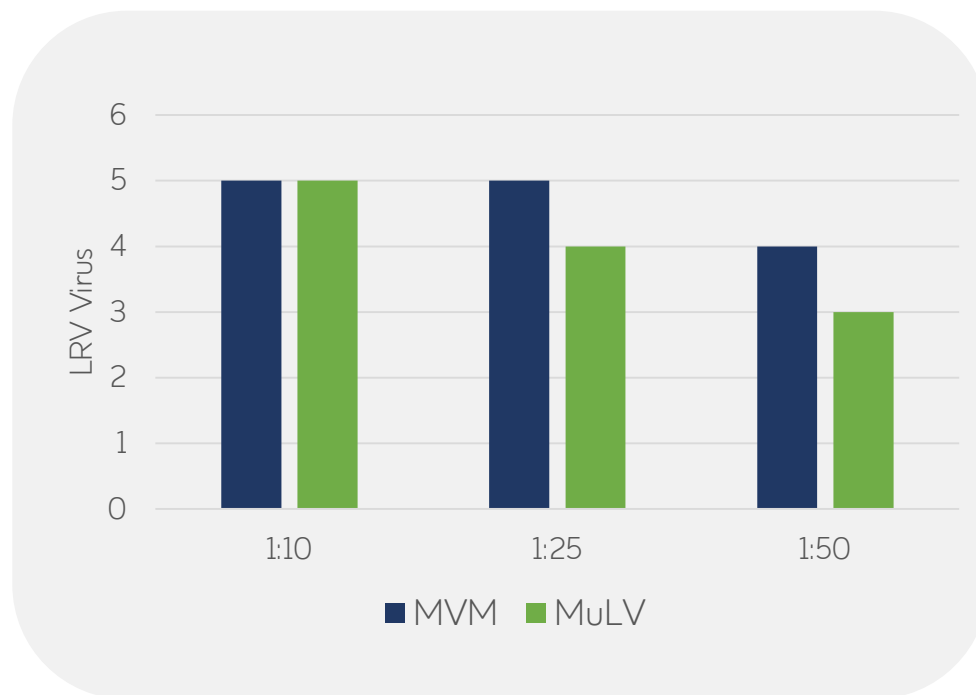
CHO-K1, DNA 500 ng/mL, HCP 175 µg/mL, IgG 2 mg/mL



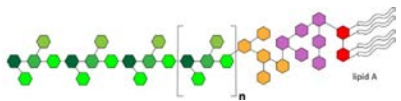
The use of MabXpure in Pipette tip format gives reliable depletion performances for very small samples.



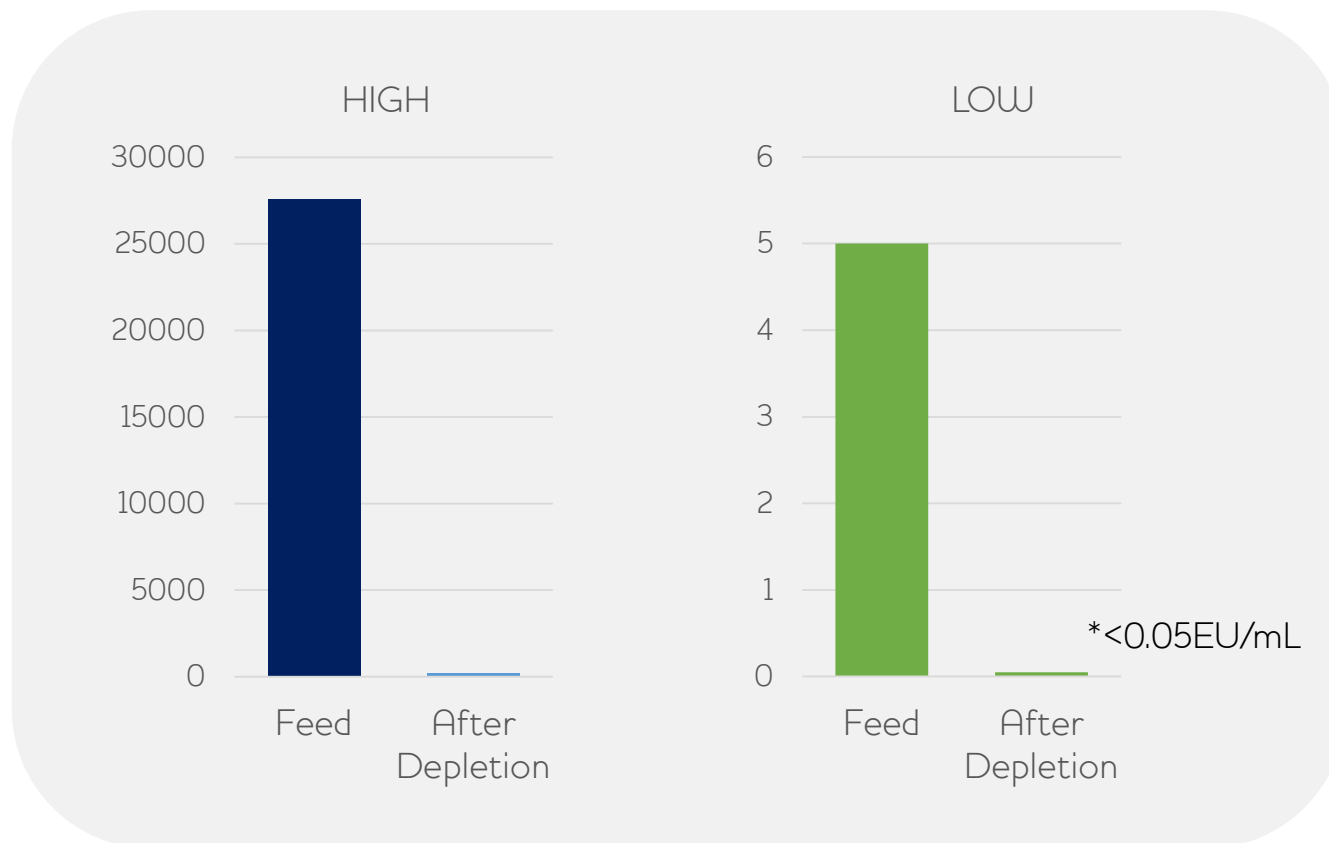
## Virus clearance MabXpure FT



MabXpure has the ability to remove viruses (up to 5 LRV). Potentially, clarification and/or polishing using MabXpure can be claimable

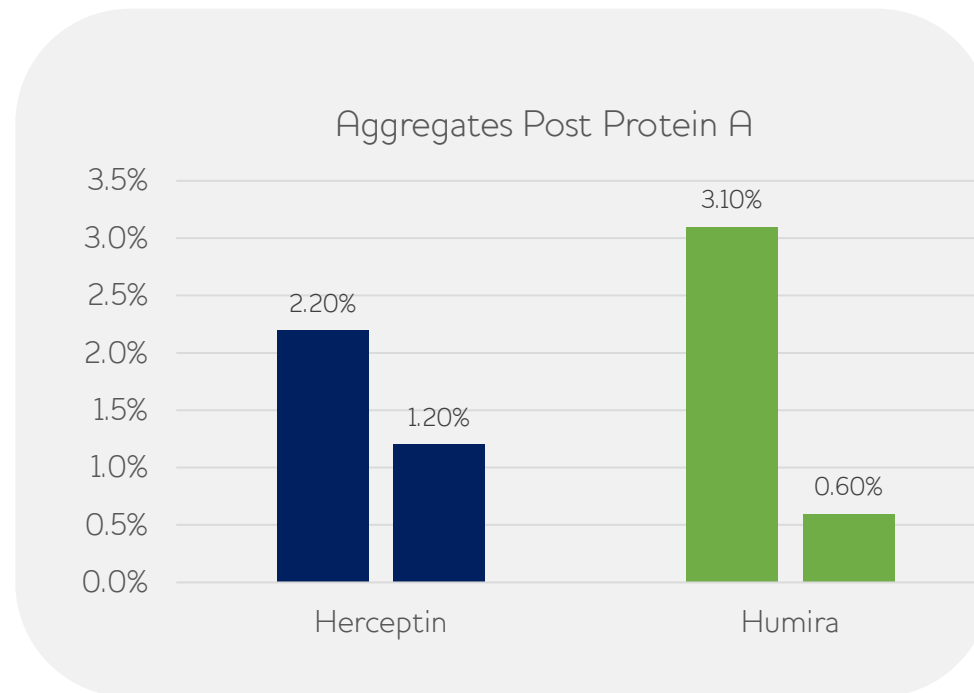


## Endotoxin clearance MabXpure



MabXpure has the ability to remove >2LRV for high and low initial concentrations

## Aggregates clearance MabXpure FT



MabXpure helps to remove aggregates after protein A. MabXpure can also be used for polishing applications

MabXpure is **first truly Single-use FlowThrough** Depletion chromatography technology

- Host Cell Proteins – Up to 1LRV @ 400.000+ ng/mL (CHO and HEK cell lines)
- DNA – 2LRV+ @ 15.000+ ng/mL
- Endotoxin – 2LRV+ @ high and low concentration (25.000 EU/mL and 5 EU/mL)
- Virus – 5LRV for MVM and XMuLV
- Aggregates (HMW) – Up to 75% removal

With activated carbon, « MabXpure + » platform depletes 98%+ impurities from harvest feed

→ **Innovative high depletion technology for HCP and Bioburden Clearance for lab/process use**

More data on Dynamic use of MabXpure for **polishing of co-eluted HCP** available at Booth 632

## DAISEP MabXPure

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Porous Silica material

35µm

Multi-modal / Size Exclusion – Anion Exchange

Commercially available

BSE-TSE free

Slurry 50/50 v/v in 20% EtOH

Regulatory support file



MabXpure bulk



DAISEP Spin XS & XL  
centrifuge tube to work  
under « Static mode »



MabXpure FT 1 mL & 5 mL  
ready to use cartridge



MabXpure FT 1500 mL  
ready to use Resin Filter  
Cartridge

谢谢

Gracias

Thank you

Grazie

Danke

спасибо

ధన్యవాదాలు

Merci



Mathieu PORTE  
Jonathan HAVARD

**Booth 528**



Fanny COSTA  
Alexandre MARGERIE  
Loïc CRESTEY  
Yasuto MORISHITA

**Booth 632**

