

SARTORIUS

Simplifying Progress



Potential Contribution of Single-Use Technologies For Processing Of Domestic Plasma Components

Prity Bengani-Lutz, Sept 2021



Disclosure Statement

- I am an employee of Sartorius Stedim Biotech


Sartorius: Innovative & Global Trusted Partner in Life Sciences Since 1870


 **400+ protein-based therapeutics**

Plasma, mAb & biosimilar

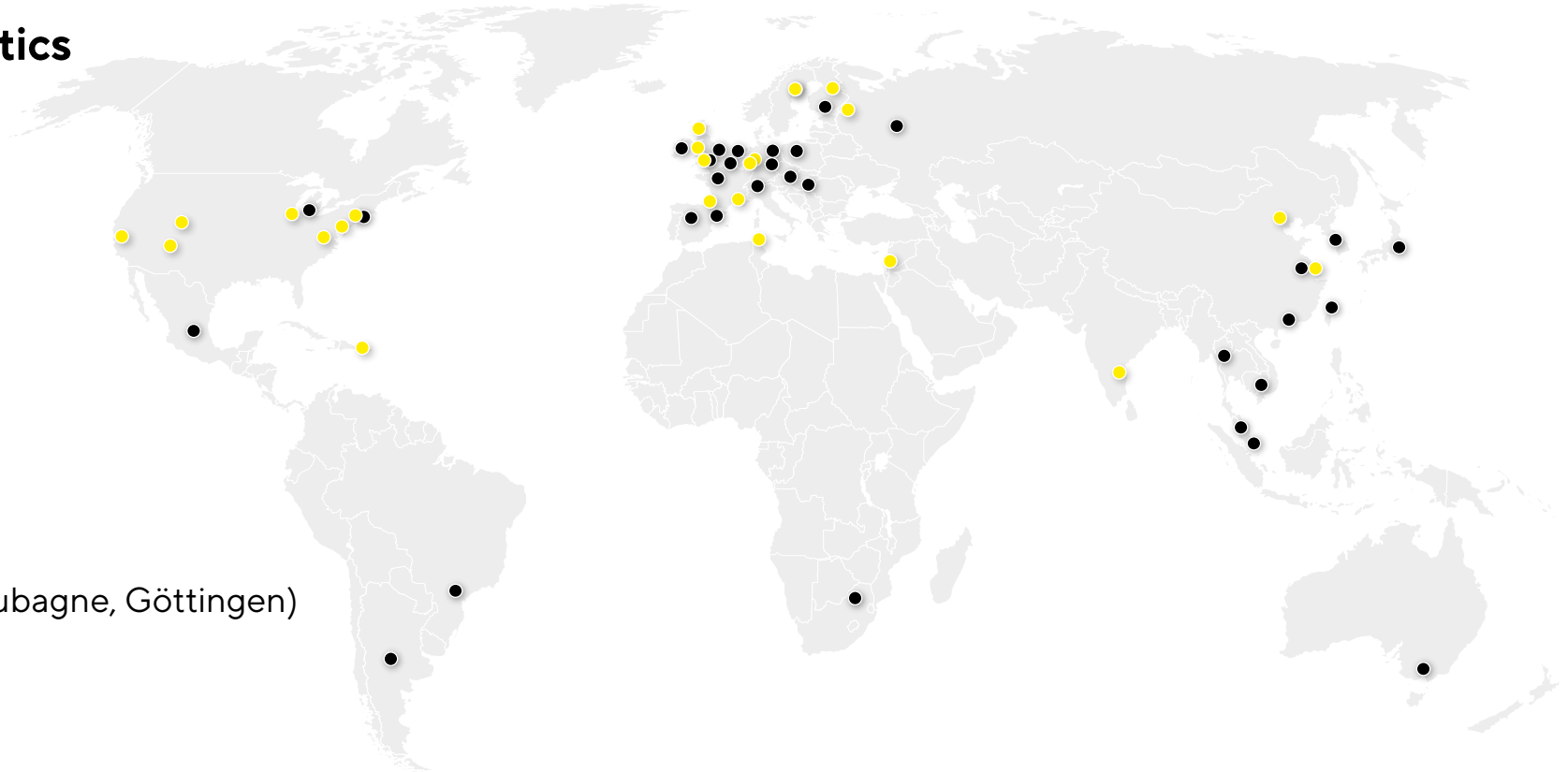
 **60+**

Locations worldwide,
headquartered in Göttingen, Germany

 **21**
Manufacturing sites

 **7**
Capacity expansions to meet demand
(Beijing, Boston, Yauco, Slovenia, UK, Aubagne, Göttingen)

 **10,600**
Employees



Agenda

Single Use vs Stainless Steel Facilities

Chromatography Challenges & Examples

Virus & Sterile Filtration

Process Support & Services



Single Use vs Stainless Steel Facilities for Plasma Processing



**Operational Flexibility
(facility & process size)**



**Increased process
efficiency**



**Reduced capital
infrastructure costs**



**Reduced time &
hardware cleaning
validation
requirements**

Sartorius Solutions for Plasma Processing From Lab Scale to Large Scale



Chromatography

HyperCel™
(CMM, STAR AX)

Sartobind®
(S, HIC, STIC, Q)

Monolithic
Column

Virus Filtration

Virosart® HC

Sterile Filtration

Sartoclean®
Midicap

Sartobran® P

- Product & Process Training
- Process Development
- Experiment Design
- Chrom Media Screening Studies
- Viral Clearance Studies

Chromatography

SU Chrom
skid

HyperCel™
(CMM, STAR AX)

Sartobind®
(S, HIC,
Q/STIC)

Monolithic
Column

Virus Filtration

Virosart® HC

FlexAct®
Modular

Sterile Filtration

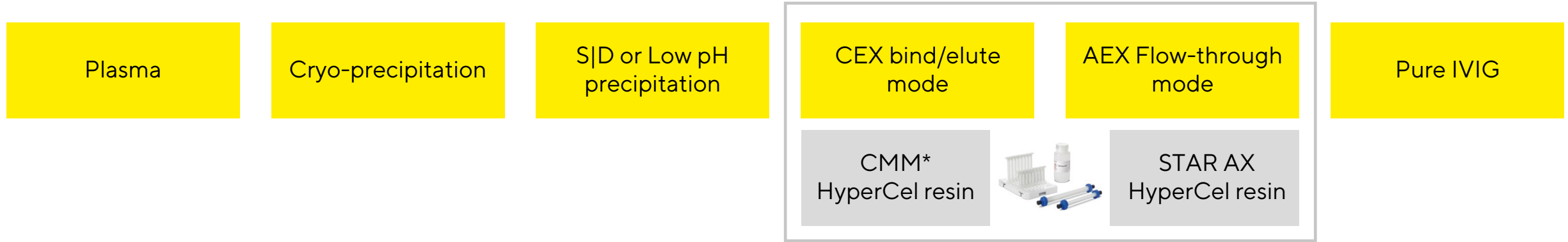
Sartoclean®
Prefilters

Sartobran® P

- Fluid Management Solutions
- Validation
- Facility Design



Chromatography Challenges in Plasma Purification



Pain points	Approaches	Benefit
<ul style="list-style-type: none"> ▪ Low yield & purity (ethanol fractionation) ▪ Costly contaminant removal ▪ Challenging removal of trace contaminants with potential for anaphylactic shock¹ or thrombogenicity² 	<ul style="list-style-type: none"> ▪ Combination of precipitation and chromatography steps ▪ Usually, combination of CEX and AEX columns 	<ul style="list-style-type: none"> ▪ Cost and time savings with no UF/DF required between CEX and AEX ▪ High yield and final purity ▪ Maintain IgG subclass distribution

¹Adverse reactions and pathogen safety of intravenous Immunoglobulin. Curr. Drug Saf. 2 (2007) 9-18.

²Wolberg, A.S., et al., Am. J. Hematol. 65 (2000) 30-34.

HyperCel Resins Enable High Recovery & 99.8% Purity of IgG

Starting material: Cryo poor plasma subjected to 5% caprylic acid treatment

	IgG Load (mg/mL sorbent)	IgG Recovery (% load)	% Total Ig		
			IgG	IgA	IgM
Post-caprylic acid	-	-	79.7	16.6	3.7
Post-S HyperCel sorbent	30	92	96.8	2.4	0.8
Post-HyperCel STAR AX sorbent	125	92	99.8	0.2	BDL

BDL: Below Detection Limit

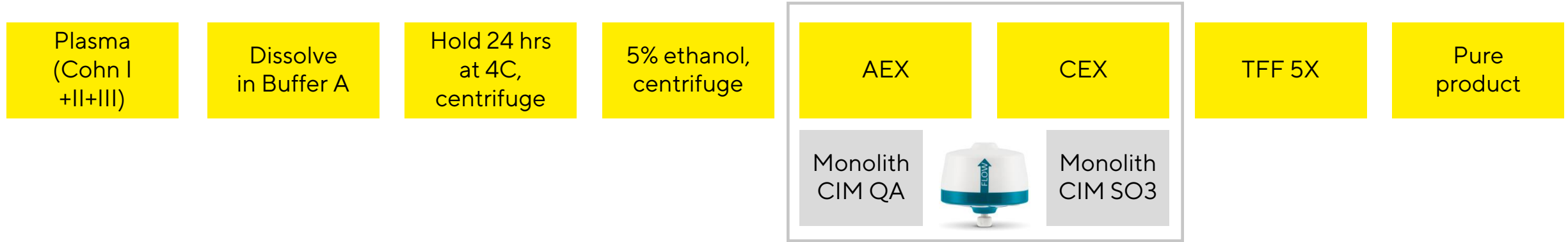
	% Total IgG Sub-Classes			
	IgG ₁	IgG ₂	IgG ₃	IgG ₄
Post-caprylic acid	69	19	2	9
Post-S HyperCel sorbent	70	19	2	8
Post-HyperCel STAR AX sorbent	70	19	2	8

IgG sub-class distribution more closely resembles plasma than other published IVIG distributions. A possible explanation is the different binding mechanism with the Post-HyperCel STAR AX adsorbent compared to DEAE- or Q- adsorbents.

- >92% recovery with Sartorius HyperCel™ Resins (CMM for CEX and STAR AX for AEX)

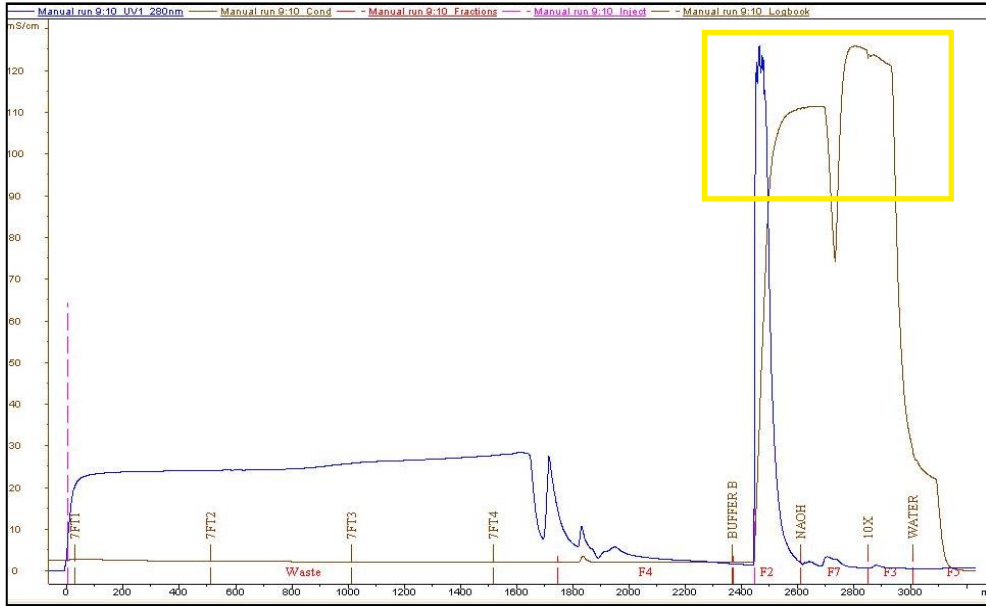
- Sartobind® S Membrane Adsorbers can also be used for further polishing & improving recovery

Cohn Paste Processing Using Monolithic Columns



Pain points	Approaches	Benefit
<ul style="list-style-type: none">▪ Purification typically from Cohn fractions I & III▪ Purification of IgM which can be used for other medicinal products	<ul style="list-style-type: none">▪ Monolith columns	<ul style="list-style-type: none">▪ Can be used with all 3 Cohn fractions▪ Very fast process, high capacity & laminar flow

Isolation of IgG from Cohn Paste (I+II+III) on 80 mL CIM AEX Column



- IgG successfully isolated from Cohn Paste
- IgA and IgM collected for further processing

Sample	Sample Volume (mL)	Protein (mg/mL)	IgA (mg/L)
Before 5% EtOH	950	21,73	5141.22
After 5% EtOH (column load)	970	22,60	1576.32
1. Consecutive run - FT fraction	105	12,83	3.05

- IgA after first run is below detection limit
- >70% of the IgM activity preserved
- Excellent aggregate removal & cost-efficiency (200+ cycles)

Viral Safety and Viral Clearance Strategy for Plasma Processing

All human medicinal products manufactured from or with the use of biological substances of human or animal origin require a virus safety concept and a virus clearance strategy

Plasma-derived medicinal products are challenging feed streams

- hydrophobic properties
- high protein concentrations
- high viscosity

Virosart® HC – Filter designed for Plasma Processing

- Non-invasive method with high protein recovery
- Performance independent of individual virus properties
- Develop process with 5 cm² area filters readily scalable



Retentive pore structure of Virosart® CPV, HC

Single-Use, High-Capacity Sterile Filters & Prefilters for Plasma Products

Materials:

- Low-binding cellulose acetate (CA)

Benefits:

- High product yield due to ultra-low unspecific adsorption
- Excellent filtration results especially for large, shear-stress sensitive proteins
- Exceptional total throughput especially for blood and plasma products

Connections:

- Filter transfer sets available for easy integration into Single-use assemblies

Sartoclean® Midicap Prefilter



Sartobran® P Filters



Pore size: 0.45 | 0.2 μm

Validation and Application Services

CONFIDENCE® Validation Service

- Extractables & Leachable
- Bacterial Challenge Test
- Chemical Compatibility
- Product Integrity Testing
- Viral Clearance Studies

Application & Value Chain Services

- Process development consultancy
- Application support for technology evaluation and implementation
- Process modeling, plant surveys
- Total cost of ownership (TCO) for technology implementation in existing/new processes facilities



Sartorius Process Consulting & Support for Plasma Processing

Product Specialists

- Application notes
- Validation guides

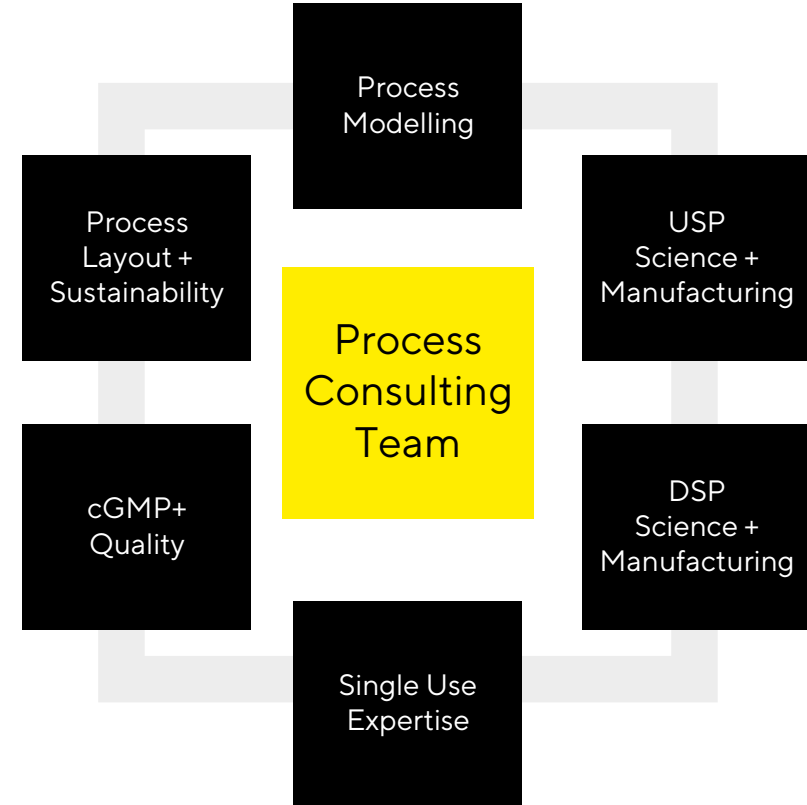
Field Application Specialists

- Onsite support for
 - Installation
 - Training
 - Validation services

Process Consultants/ Engineers

- Facility design
- Room classification
- Room segregation

Contact your local Sartorius Sales rep for more details



Thank You & Contact Information



prity.bengani-lutz@Sartorius.com

www.sartorius.com

<https://www.sartorius.com/en/applications/biopharmaceutical-manufacturing/blood-and-plasma>

SARTORIUS

