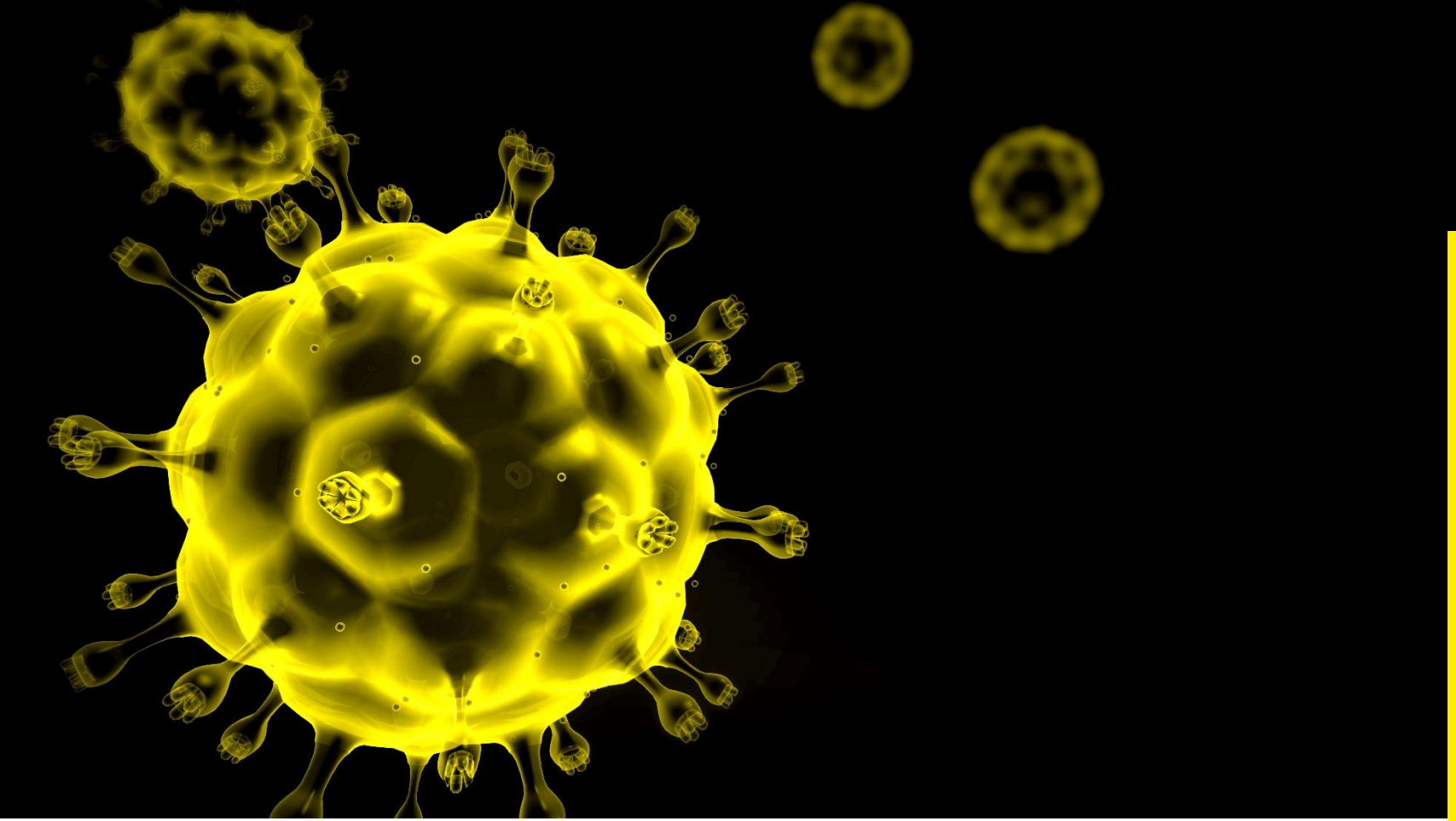

Simplifying Progress

Accelerated Vaccine manufacturing using Sartorius Solutions

Viral vector- based vaccines

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Agenda

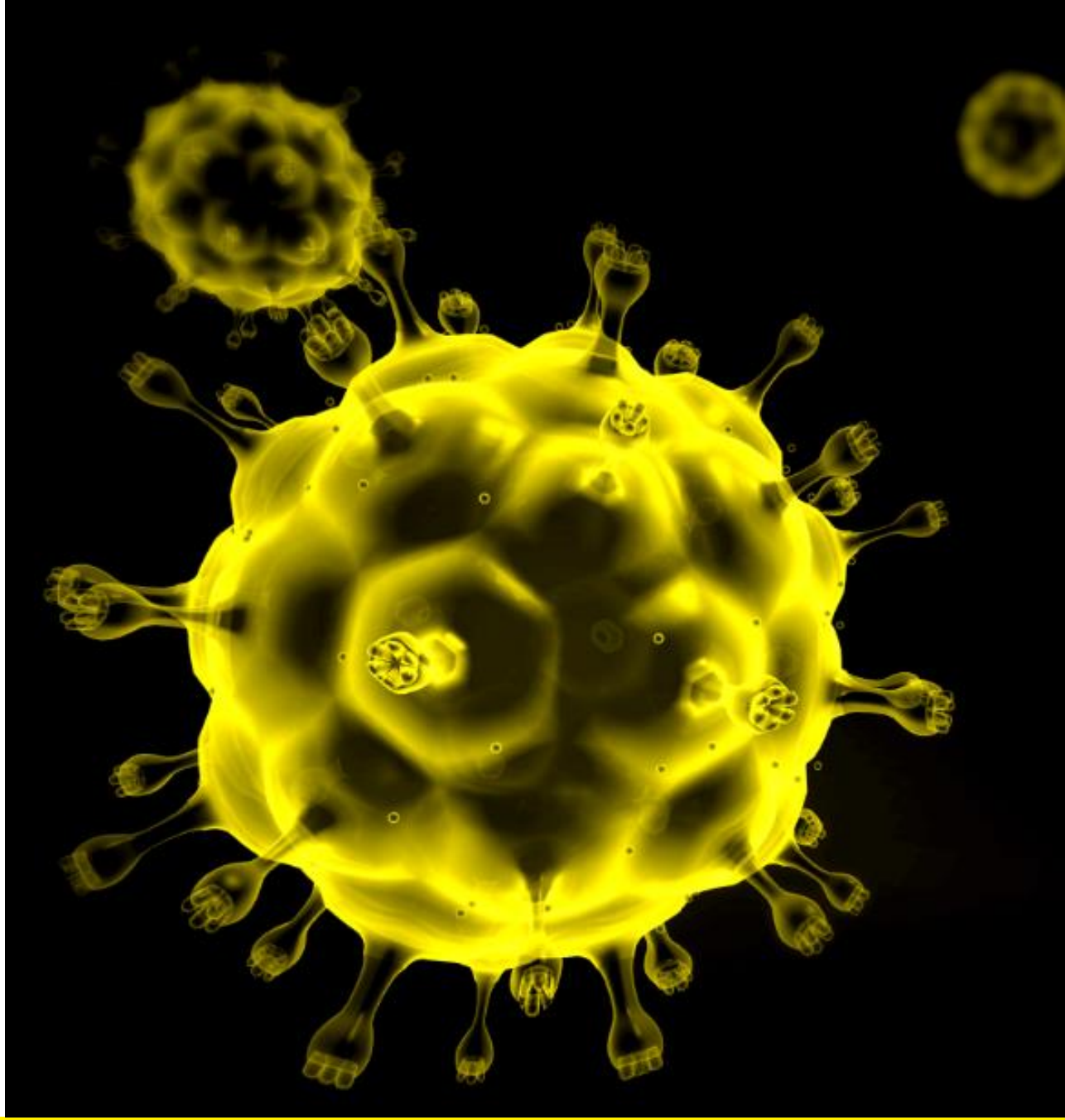
Introduction

Seamless **Scalable Upstream Solutions**

Flexible **Downstream Solutions**

Reliable Analytical Solutions

Conclusion



Key Drivers- Vaccine development and manufacturing

Needs

Speed to Clinic | Market

- Shorter process development timelines
- Decrease in time from Preclinical to clinical trials.
- Increase use of CMOs and technology transfer

Process Improvement

- Increase productivity to reduce scale up requirements
- Process robustness from early clinical phase
- Increased regulatory expectations

Flexible Processes

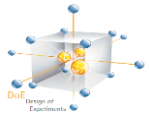
- Flexible ballroom for product changeover
- Localized production in low middle income countries
- closed processes and ability to produce larges virus

Set Your Success from Early Process Development

Cell line & Media Selection/Cell Banking | Cell Expansion | Viral Vector Production | Cell Lysis

Ambr® 15

MODDE® DOE software



Fill-it

Ambr® 250 HT

Ambr® 250 Modular

Univessel® & Biostat®

BIOSTAT® RM

Cell culture & transfection optimization

Sterile Filtration

Sartopore® Platinum / Sartopore® 2

Chromatography

Resins in Robo & PRC Pre-packed Columns

Sartobind®

CIM Monolith

TFF: Concentration & Buffer exchange

Sartocon® Cassette

Ambr® Crossflow

Harvest

Sartopure® PP3
Sartopore® 2 XLG

Sterile Filtration | UF/DF – Final Formulation | Polishing | Purification | UF/DF – Buffer adjustment | Clarification

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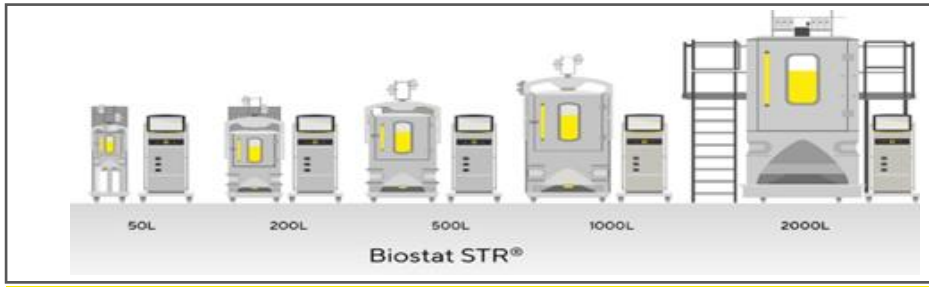
Solutions for Production Scale manufacturing- Viral Vaccines

Cell Expansion | Viral Vector Production | Cell Lysis

Mycap®

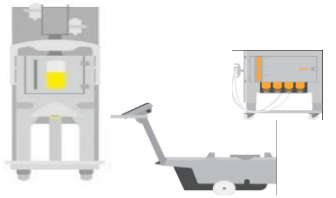
Biostat RM®

Seed cultivation



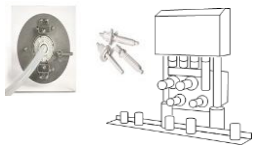
Scalable production

Flexsafe® Pro Mixer



Cell Lysis

Final Filling



OctoPlus FF®

Sterile Filtration

Sartopore® Platinum / Sartopore® 2

Chromatography

Resolute® Flowdrive SU | BioSMB | Resolute® columns

Concentration / Diafiltration

Sartoflow® 1000 & 4500 | Sartocon® SC | Flexact® Modular

Harvest

Sartopure® PP3 & Sartopore® 2 XLG

Final Filling | Sterile Filtration | UF/DF – Final Formulation | Polishing | Purification | UF/DF – Buffer adjustment | Clarification

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Proprietary Cell Banking, Media and Testing Services

High quality cell banking, media and testing services are essential for rapidly moving into phase I cGMP production

Cell Banking & Characterization	Integrated Cell Banking, Testing & Characterization Package	▪ HEK293 MCB of 500 vials with 12 mio cells per vial in ≤ 5 months ▪ HEK293 WCB in ≤ 3 months ▪ HEK293 Master Cell Bank Biosafety Testing and Characterization in < 10 weeks ▪Vero and MDCK - testing and characterization
Cell Culture Development	Viral Vector Testing & Custom Assay Development	▪ Platform pre-qualified cGMP assays from early clinical to commercial lot release ▪ Custom PCR and ELISA assay development in < 6 weeks
Scale-up and Production	Customized 4Cell® Media Solutions	▪Off the shelf and Custom proprietary HEK293 media manufacturing

PCR: Polymerase Chain Reaction, ELISA: enzyme-linked immunosorbent assay

High-Throughput and Scalable Stirred Tank Bioreactor Solutions for USP- Process Development

Cell Banking & Characterization

Process Development

Scale-up and Production

Ambr® 15	Ambr® 250 Modular	Ambr® 250 HT	Univessel® & Biostat®
			
24/48 bioreactors 10-15mL working	Up to 8 bioreactors 100-250mL	12/24 bioreactors 100-250mL	Single Use/ Multi-use bioreactors 1L – 10L

Ambr® 15 & 250, the only solutions that offers:

- Scalable, multiparallel, automated functionality
- Proven optimization of your process with HEK293T cell lines
  - Cell line screening & clone selection for stable expression
  - Optimization of transfection conditions
  - Media & process development
  - Advanced process control through integration of inline analytics of BioPAT® toolbox
- Easy to connect with MODDE® DoE software

Biostat® bbenchtop bioreactors; right functionality for your specific process development:

- Univessel® available from 1 – 10L
- The control unit can operate any combination from Univessel® Glass to Univessel® SU
- Holder for the Univessel® SU has built-in optical sensor interfaces for pH and DO monitoring and control
- Integrate with inline analytics of BioPAT® toolbox
- Easy to connect with BioPAT® MFCS to monitor process data

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Get Ready to Safely Start Large Scale Production

Biostat®

Cell Banking & Characterization

Cell Culture Development

Scale-up and Production

Optimize your cell culture & rely on proven scalability

- Geometrical similarity of vessel design
- Consistent mixing strategies
- Simplify scale down & scale up studies
- Mitigate risks during process transfers
- Scalable process from 250ml to 2000L

Process monitoring & control with BioPAT®

- BioPAT® Spectro facilitates and improves the model Building and data Management process with Raman spectroscopy
- BioPAT® Trace ensures simultaneous online monitoring of glucose and lactate
- BioPAT®ViaMass enables real-time determination of viable biomass

Ensure process & operator safety with Flexsafe®

From seed train to production, Flexsafe® RM and Flexsafe STR®:

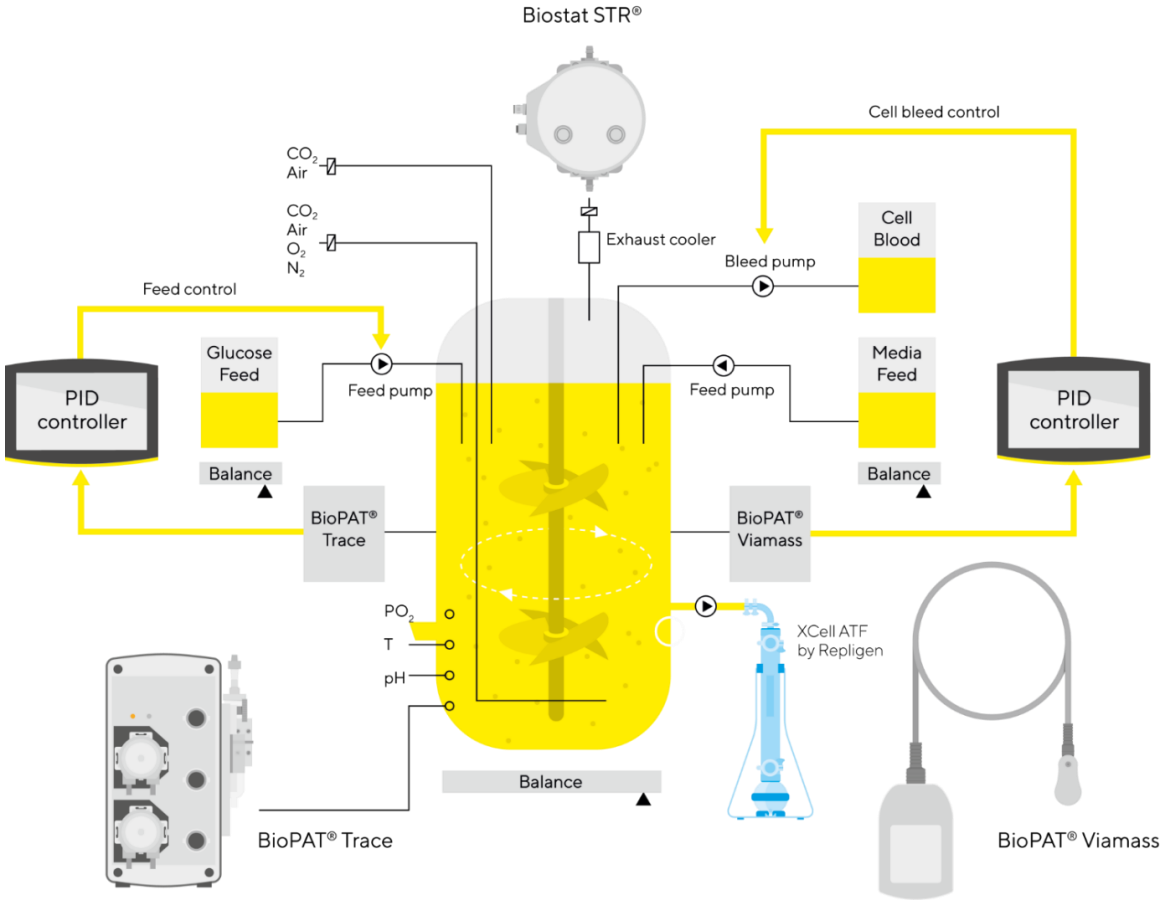
- Superior robustness
- Point of use leak test
- Assurance of supply
- Excellent cell growth
- Consistent E&L profiles

Real-Time Data for Outstanding Process Control With BioPAT® Toolbox

Cell Banking & Characterization

Cell Culture Development

Scale-up and Production



With inline and online process analyzers, you can achieve:

- Robust processes
- High-quality and consistent production
- Good understanding of key production steps
- Raman spectroscopy to analyze various tests online (upcoming)

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Avoiding Virus Adsorption during Harvest, Clarification and Sterile Filtration

- Harvest & Clarification (Centrifugation/ Filtration)
- Buffer Exchange (UF/DF1)
- Chromatography-Capture
- Chromatography-Polishing
- Buffer Exchange (UF/DF 2)
- Sterile filtration

Harvest/ Clarification

Sartopure® PP3/GF+

- Cell & cell debris removal
- Low adsorption of virus
- High viral vector recovery
- High capacity

Sartoclear® Depth Filter

- Good performance in removal of small contaminants and DNA
- High capacity
- Suitable for high cell density culture
- pH and conductivity to be optimized to increase virus recovery

Sterile Filtration

Sartopore® 2/ Platinum

- Low adsorption of virus
- High infectious viral vector recovery
- Available as standard cartridges, in a closed capsule format, as filter transfer sets and in MaxiCaps® MR format

A complete range of Chromatography System for downstream processing

- Harvest & Clarification (Centrifugation/ Filtration)
- Buffer Exchange (UF/DF1)
- Chromatography-Capture
- Chromatography-Polishing
- Buffer Exchange (UF/DF 2)
- Sterile filtration

Chromatography Columns/ Media	 Columns	 Resins	 Monoliths	 Membrane adsorbers	
Chromatography Systems	 PK/PKP 	 MU RCC	 Allegro SU	 BioSMB 	

Chromatography Consumables from PD to commercial scale

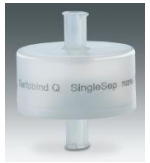
- Harvest & Clarification (Centrifugation/ Filtration)
- Concentration and Buffer Exchange (UF/DF1)
- Chromatography Capture
- Chromatography-Polishing
- Concentration and Buffer Exchange (UF/DF 2)
- Sterile Filtration

Sartobind® Q Membrane

- Bind & elute capture step for protein and DNA removal
- High capacity and flow rates
- Low buffer consumption and footprint processes
- Available in capsules and cassette format to meet process scales from PD to commercial manufacturing

HyperCel Resins

- Both IEX and Hydrophobic property for good removal of impurities
- Reduced buffer consumption due to no pH/ conditions
- Broad range of pH and conductivity



Sartobind 96 Well Plate Sartobind Nano ← Sartobind Capsules and Cassettes →

Discovery → Preclinical → Preclinical – Phase I → Phase II-III-Commercial

R&D | PD | Pilot | Large

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DSP-UF/DF Solution: From PD to Commercial Scale

Harvest & Clarification (Centrifugation/ Filtration)

Buffer Exchange (UF/DF1)

Chromatography-Capture

Chromatography-Polishing

Buffer Exchange (UF/DF 2)

Sterile filtration

Multiuse systems

Ambr® Crossflow

Sartoflow® Smart

Sartoflow® Advanced

R&D (Discovery) → PD (Preclinical) → Proof of Concept-Pilot → Pilot to commercial

Single use systems

Sartoflow® 150

Sartoflow® 1000

Flexact®

Sartoflow® 4500

Consumables

Sartocon® slice 50

Sartocon® slice

Sartocon® SC

Sartoflow® single-use Flow Kits

Sartocon® Self Contained Filter and Bag Loop Assemblies

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Analytical Chromatography Portfolio

CIMac™

Designed for fast and reproducible HPLC monitoring and quantitation of proteins, viruses, pDNA, and other large biomolecules, they allow you to achieve rapid, high-resolution and flow-independent separations in a matter of minutes.

CIMac™ Analytical Columns

Bed volume 100 µL.

Optimised for best resolution

PAT fix™ HPLC

Ideal system for routine gradient separations that enables you to do every analytical task. Equipped with bio-inert ceramic heads, it is deliberately tailored to meet the demands of analytical applications covering a wide range of biomolecules. Its highly sensitive and fast multi-wavelength detector enables detection of component peaks even in very fast gradients.

PATfix™ HPLC Systems

For process control analysis

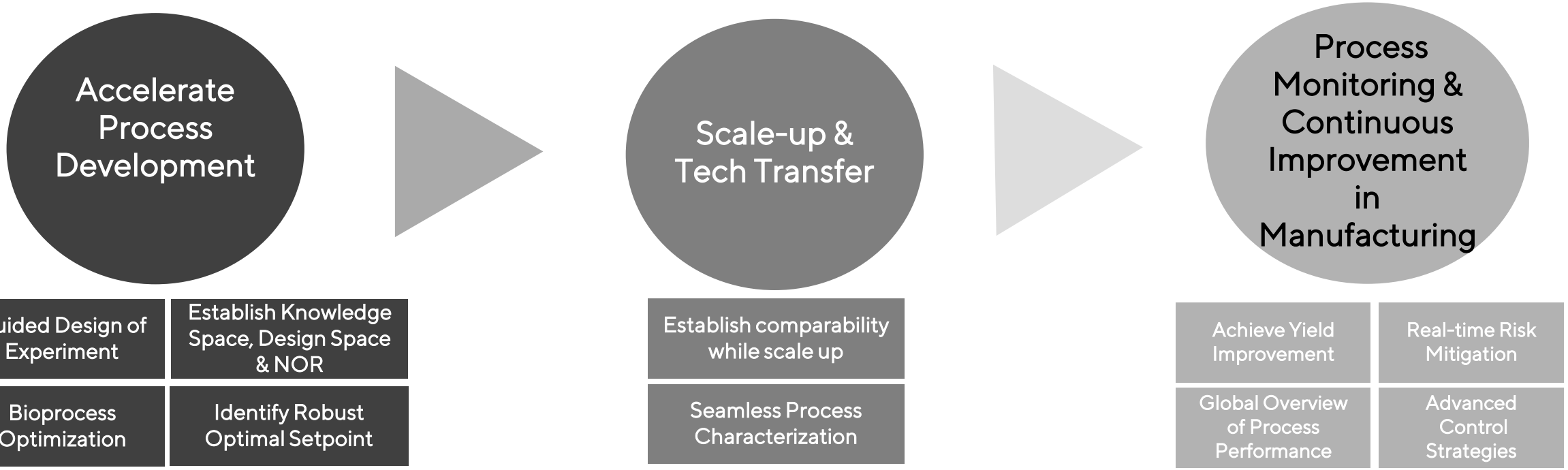
Work with CIMac™ analytical columns

Addressing Major Viral Vector Challenges with Data Analytics

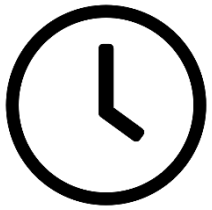
Systematically approach process development studies and reduce the numbers of experiments run

Accelerate scale-up and de-risk tech transfer while ensuring process robustness

Monitor and control manufacturing processes to delivery high quality vaccine

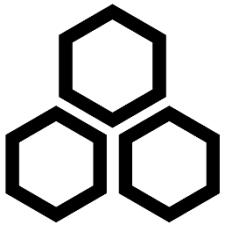


Start the Development with the Aim in Mind



Speed to Clinic | Market

Process Improvement



Flexible Processes

Increasing the viral titer with high throughput tools for process development that ensure process scalability and robustness

Selecting the appropriate technologies along the DSP to ensure highest virus recovery and purity

Single use technology to improve efficiency and flexibility

Monitor and control your process with rapid viral quantification, PAT and MVDA data analysis software to improve process efficiency and product consistency

Thank you.

Raman Rani
Manager- Application services

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