Accelerated Vaccine manufacturing using Sartorius Solutions
Viral vector-based vaccines
Agenda

Introduction

Seamless **Scalable Upstream Solutions**

Flexible **Downstream Solutions**

Reliable Analytical Solutions

Conclusion
Key Drivers- Vaccine development and manufacturing

**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 large virus

Needs
Set Your Success from Early Process Development

- Cell line & Media Selection/Cell Banking
  - Ambr® 15
  - MODDE® DOE software
  - Fill-it

- Cell Expansion
  - Ambr® 250 HT

- Viral Vector Production
  - Ambr® 250 Modular
  - Univessel® & Biostat®

- Cell Lysis
  - BIOSTAT® RM

Introduction

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
Introduction

Solutions for Production Scale manufacturing - Viral Vaccines

Cell Expansion
- Mycap®
- Biostat RM®

Viral Vector Production
- Scalable production

Cell Lysis
- Flexsafe® Pro Mixer

Seed cultivation

Introduction

Sartopore® Platinum / Sartopore® 2

Final Filling
- OctoPlus FF®
- Sartopure® PP3 & Sartopore® 2 XLG

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
- UF/DF – Final Formulation
- Polishing
- Purification
- UF/DF – Buffer adjustment

Clarification
Seamless Scalable Upstream Solutions

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

- 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

- 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

- 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

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® benchtop 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
Get Ready to Safely Start Large Scale Production

Seamless Scalable Upstream Solutions

- 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
- 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

Optimize your cell culture & rely on proven scalability

Process monitoring & control with BioPAT®

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

Cell Banking & Characterization
Cell Culture Development
Scale-up and Production

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Seamless Scalable Upstream Solutions

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

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)
Avoiding Virus Adsorption during Harvest, Clarification and Sterile Filtration

<table>
<thead>
<tr>
<th>Harvest &amp; Clarification (Centrifugation/Filtration)</th>
<th>Harvest/Clarification</th>
<th>Sterile Filtration</th>
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<tbody>
<tr>
<td>Buffer Exchange (UF/DF1)</td>
<td>Sartopure® PP3/GF+</td>
<td>Sartopore® 2/ Platinum</td>
</tr>
<tr>
<td>Chromatography-Capture</td>
<td>Sartoclear® Depth Filter</td>
<td><em>Low adsorption of virus</em></td>
</tr>
<tr>
<td>Chromatography-Polishing</td>
<td></td>
<td><em>High infectious viral vector recovery</em></td>
</tr>
<tr>
<td>Buffer Exchange (UF/DF 2)</td>
<td></td>
<td><em>Available as standard cartridges, in a closed capsule format, as filter transfer sets and in MaxiCaps® MR format</em></td>
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<tr>
<td>Sterile filtration</td>
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</tbody>
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- **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

- **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**

<table>
<thead>
<tr>
<th>Chromatography System</th>
<th>Columns</th>
<th>Resins</th>
<th>Monoliths</th>
<th>Membrane adsorbers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chromatography Columns/Media</td>
<td>PK/PKP</td>
<td>MU RCC</td>
<td>Allegro SU</td>
<td>BioSMB</td>
</tr>
</tbody>
</table>
Chromatography Consumables from PD to commercial scale

**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

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Flexible Downstream Solutions

Harvest & Clarification (Centrifugation/Filtration)

Concentration and Buffer Exchange (UF/DF1)

Chromatography Capture

Chromatography-Polishing

Concentration and Buffer Exchange (UF/DF 2)

Sterile Filtration

Sartobind 96 Well Plate

Sartobind Nano

Sartobind Capsules and Cassettes

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

R&D  PD  Pilot  Large
DSP-UF/DF Solution: From PD to Commercial Scale

Flexible Downstream Solutions

- Harvest & Clarification (Centrifugation/Filtration)
- Buffer Exchange (UF/DF 1)
- Chromatography-Capture
- Chromatography-Polishing
- Buffer Exchange (UF/DF 2)
- Sterile filtration

Multiuse systems:
- Ambr® Crossflow
- Sartoflow® Smart
- Sartoflow® Advanced

Single use systems:
- Sartoflow® 150
- Sartoflow® 1000
- Flexact®
- Sartoflow® 4500

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

Consumables:
- Sartocon® slice 50
- Sartocon® slice
- Sartocon® SC
- Sartoflow® single-use Flow Kits
- Sartocon® Self Contained Filter and Bag Loop Assemblies
Reliable Analytical Solutions

Analytical Chromatography Portfolio

ClMac™

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.

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.
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 deliver high quality vaccine

**Accelerate Process Development**
- Guided Design of Experiment
- Bioprocess Optimization
- Establish Knowledge Space, Design Space & NOR
- Identify Robust Optimal Setpoint

**Scale-up & Tech Transfer**
- Establish comparability while scale up
- Seamless Process Characterization

**Monitor and control manufacturing processes to deliver high quality vaccine**
- Achieve Yield Improvement
- Real-time Risk Mitigation
- Global Overview of Process Performance
- Advanced Control Strategies

**Tools**
- MODDE® DOE
- SIMCA® MVDA
- SIMCA®-online
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