Fast Trak Capabilities

Welcome DCVMN delegates!

October 19, 2017

GE Healthcare's Life Sciences

Accelerating precision medicine with tools for biotechnology R&D, biopharma manufacturing, cell therapy and regenerative medicine, diagnostic imaging, molecular and precision diagnostics.

Core imaging

Diagnostic imaging agents

- Nuclear medicine
- PET tracers
- DATSCAN™
- OMNIPAQUE™
- VISIPAQUE™

BioProcess

Tools for biopharma manufacturing:

- Single-use cell culture
- Chromatography
- KUBio™
- HyClone™
- Xcellerex™
- WAVE

Cell therapy

Solutions and expertise for scaled-out cell therapy workflows:

- Cell culture media and systems
- Data software and analytics
- Xuri™

Genomics & cellular research

Understanding life at the molecular level:

- Cell assays
- Gene modulation
- Molecular biology
- Human forensics
- Whatman™
- DeltaVision™

Purification & analysis

Tools for protein purification and analytics:

- Chromatography media
- Protein interactions
- Biacore™
- Amersham™

Five product business units • ~10,500 people • 100+ countries • UK HQ
Manufacturing, research and development in US, Europe and Asia

Fast Trak mitigates growth-limiting realities

Overcoming bioprocessing bottlenecks and gaining expertise in critical manufacturing techniques ensures long term success and speed to market

OPPORTUNITY

- New therapeutic protein with great looking efficacy profile
- Potential to enter market with new biologic or biosimilar
- Take advantage of single-use technology to reduce capital expense/running costs

Research → Process Development → Optimization → Scale up → Tech Transfer

REALITY

- Little to no expertise in protein process development, scale up, conversion to single-use enabling technologies
- Resources are limited, timing is critical
- No production facility
- In country, for country; managing local construction/RA
- No data on cross platform validation

Fast Trak

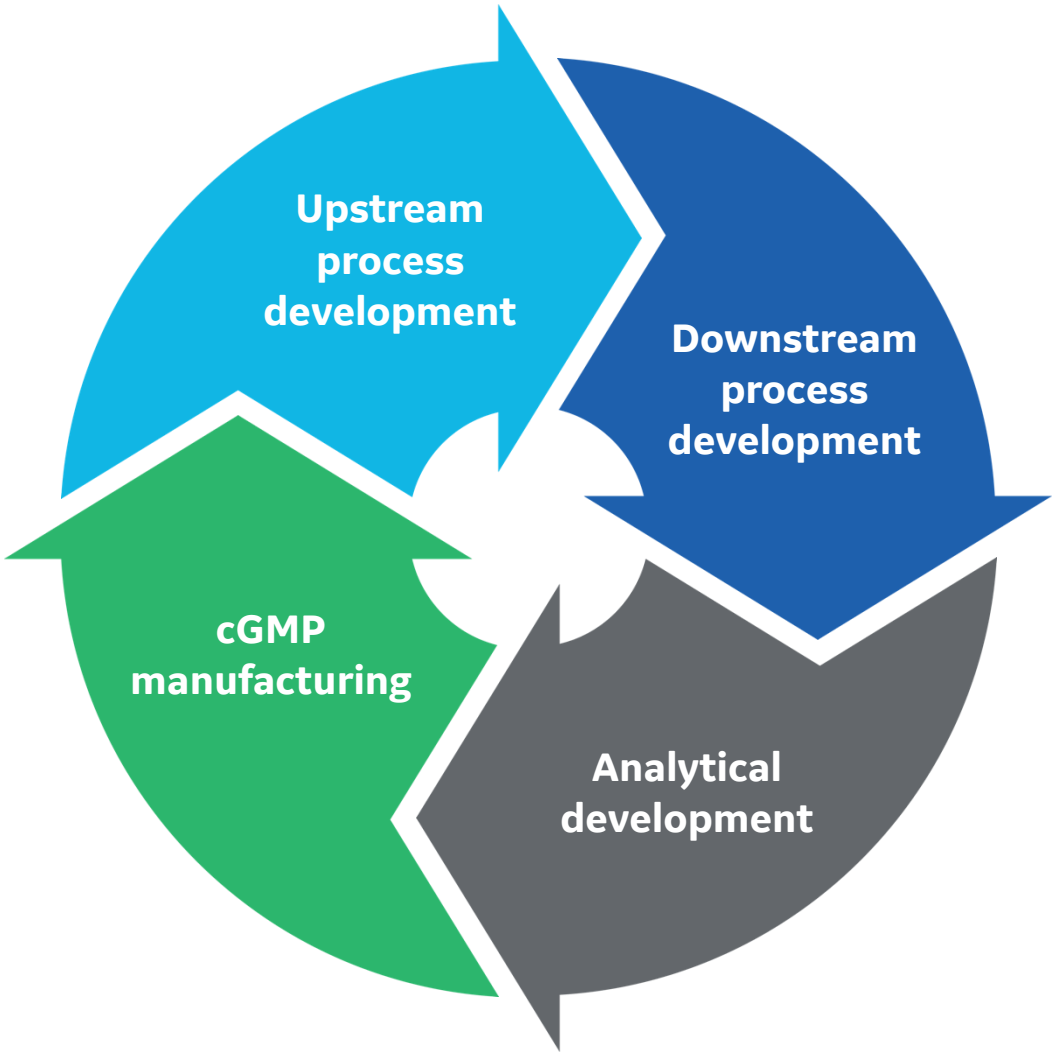
Accelerating molecules to market

- Accumulative experience
  - Time-efficient process development services
- Time tested training courses
  - Hands-on experience that reinforces concepts
- Identical platform base
  - Seamless bridging to manufacturing services
- Concurrent construction/validation
  - Transfer to your facility, a CMO, greenfield facility or KUBio™

GE's Fast Trak services

With GE's worldwide footprint, you not only go faster to market, you can also go further

Process development services



- End-to-end process development
- Process scale-up and proof of concept
- Bioreactor process optimization
- End-to-end downstream development
- Resin screening and optimization
- Design of experiments (DoE)
- High-throughput process development (HTPD)
- Resin cleaning in place (CIP) studies
- Resin lifetime studies
- Methods development & transfer
- Methods qualification
- Reference standard characterization
- Stability studies
- Lot release testing
- cGMP BSL1 – from 10 L to 2000 L
- cGMP BSL2 – from 10 L to 500 L

Process transfer to customer site

Local Fast Trak services teams support process transfer to emerging regions, sourcing of local raw materials and understand local government and regulatory requirements

Fask Trak Manufacturing Services

At GE

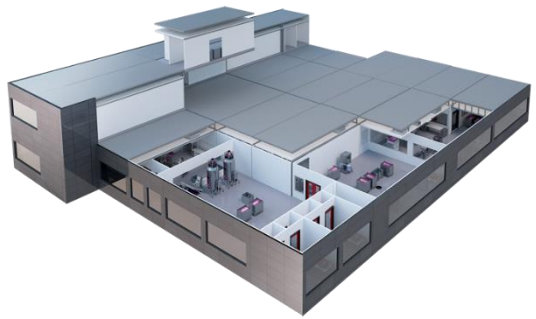
Process development
Analytical development
Scale-up

Documentation preparation
cGMP manufacturing
Train/educate customer team

TransPlant

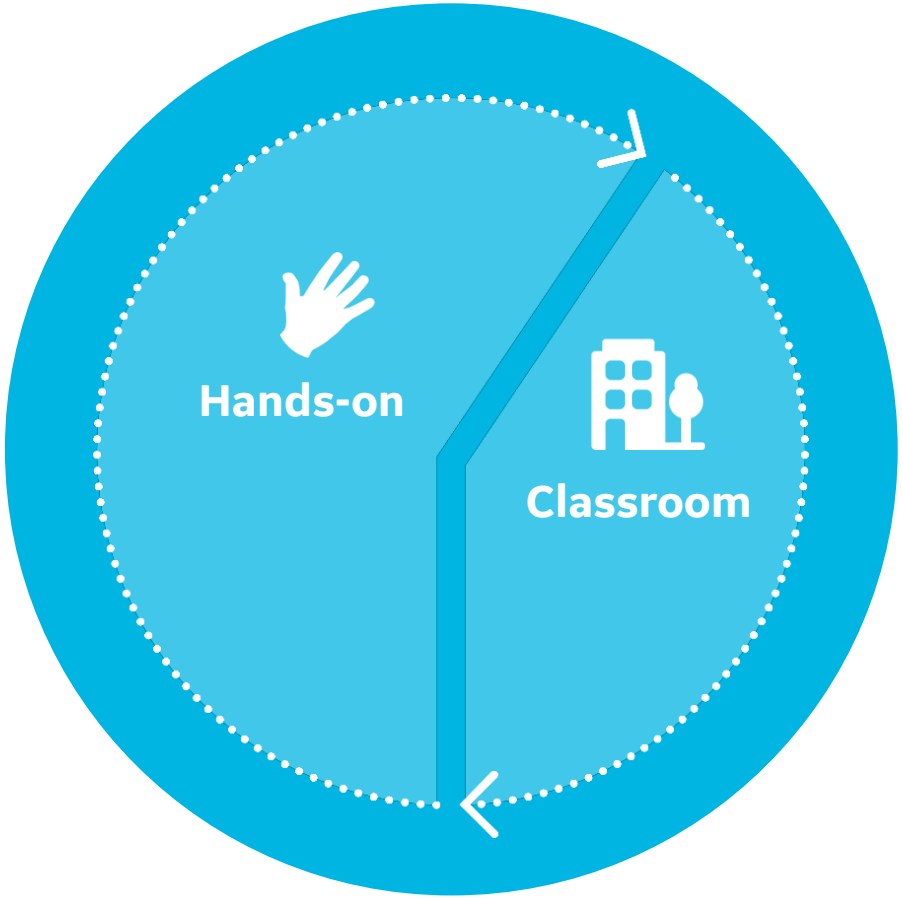
Process | **Analytical** | **Documentation** | **Training** | **Start-up**

FlexFactory™ platform
KUBio™ facility
Contrast manufacturer
Customer facility



cGMP = current good manufacturing practices

Training and education



We offer training courses in specialist manufacturing techniques at our global training centers

- Classroom, on-site, and online education
- Courses held at regional centers around the globe
- Global curricula in local languages

Fast Trak standard courses 2017 schedule

		USA, Marlborough, MA	India, Bangalore	Sweden, Uppsala	Germany, Munich	Turkey, Istanbul	China, Shanghai	Singapore	Japan, Tokyo	South Korea, Songdo
Upstream processing										
CELL1	Advanced bioreactor cultivation technology	Feb 27–Mar 2	–	May 16–19 Oct 10–13	–	–	–	Mar 28–31	Dec 5–8	Apr 18–21
CELL2	Advanced bioreactor cultivation and scale-up	–	–	–	–	–	Apr 18–21 Dec 5–8	–	–	–
Downstream processing										
DEV1	Introduction to downstream techniques and bioprocessing	Mar 14–16	Jun 20–22	Apr 4–6	Feb 20–22 Oct 24–26	Oct 10–12	–	–	Sep 7–8	May 23–25
DEV2	Downstream bioprocess development	Jun 12–16	Jul 10–14	Mar 13–17	–	–	Jul 3–7	Sep 11–15	–	Oct 16–20
DEV4	Bioprocess scale-up and technology transfer	Aug 15–17	Nov 7–9	Sep 5–7	–	–	Oct 17–19	–	–	Nov 29-Dec 1
HTPD1	Introduction to high-throughput process development—workshop	Apr 4–6	Oct 24–26	–	–	–	–	–	–	–
DOE1	Introduction to design of experiments	May 16–18	Jun 13–15	Jun 14–16	May 3–4 Nov 23–24	–	Mar 14–16 Nov 14–16	Sep 19–21	–	–
MAB1	Downstream bioprocessing of monoclonal antibodies	–	–	–	–	Nov 21–24	May 16–19	–	Jun 7–9	–
Techniques										
SUM1	Single-use manufacturing technologies	–	–	–	–	–	–	–	–	–
COL1	Large-scale column packing	Apr 25–27 Sep 12–14	–	Mar 21–23 Sep 19–21	–	–	–	–	Nov 9–10	Jul 4–6
COL2	Basic Column packing Bangalore, India—facility only	–	Feb 7–9	–	Jul 10–12	–	–	Jun 13–15	–	–
MEM1	Bioprocessing using membrane separations	May 2–4		Nov 7–9		–	–	–	–	–
UNICORN™ system control										
UNI1	Advanced UNICORN system control for chromatography systems	Oct 17–19	Mar 7–9	Feb 28–Mar 2	–	–	–	Apr 4–6	–	Sep 4–6
Quality assurance										
QBD1	Quality by design—workshop	–	–	–	–	–	–	–	–	–
VWS1	Validation—workshop	–	–	–	–	–	–	–	Jul 21	–

Please contact your regional Fast Trak center for custom courses.
Contact regional Fast Trak centers for latest calendar updates

Customized training and education

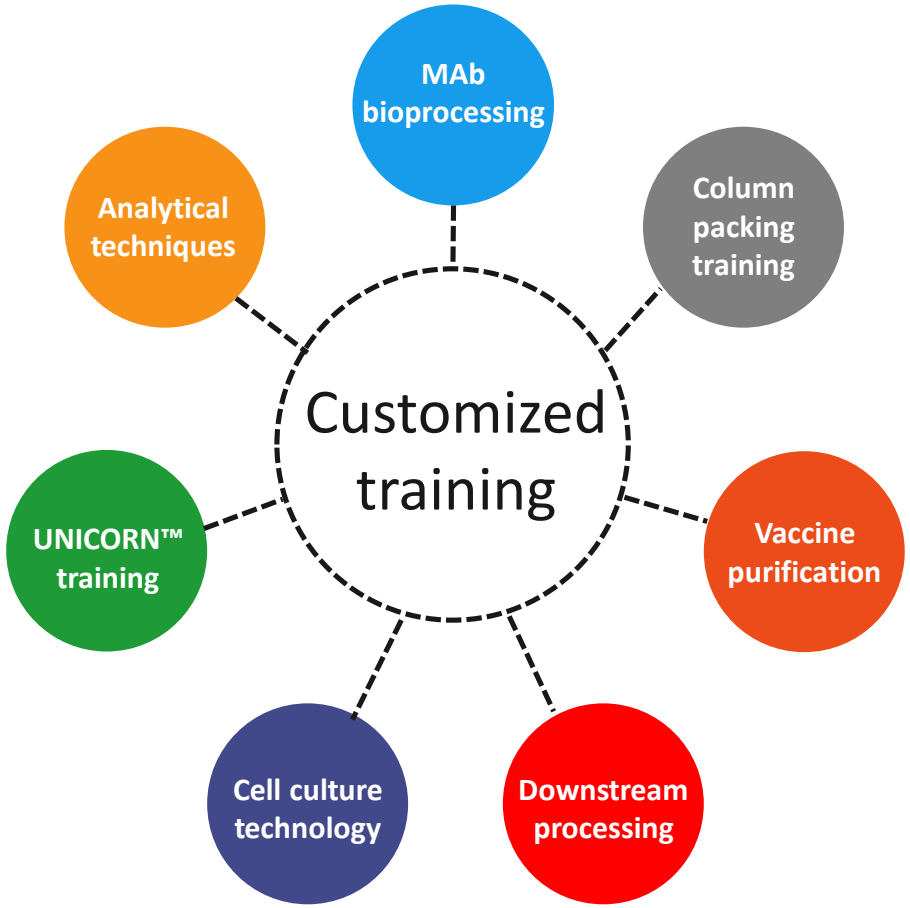
Concept: Modular and tailor-made content

Duration: From days to weeks

Location: Fast Trak center/customer site

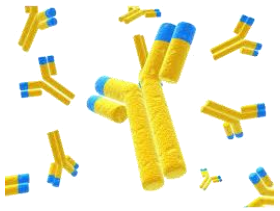
Equipment: Specific pool provided by Fast Trak

Trainer: Fast Trak, R&D/Application team

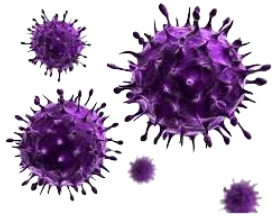


Fast Trak experience

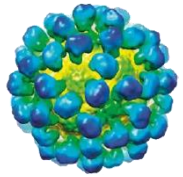
Monoclonal antibodies



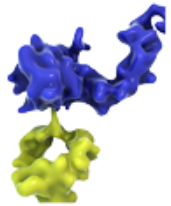
Viruses



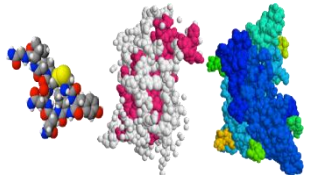
Virus-like particles



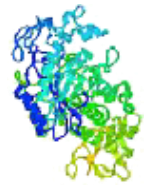
Fusion proteins



Hormones



Enzymes



- 300 years of collective industry experience (Fast Trak Leadership Team)
- 100 production campaigns completed
- 500 scientists trained annually
- 17 different expression systems used
- 17 virus clearance studies completed
- Fast Trak started 30 years ago

APAC Fast Trak Center

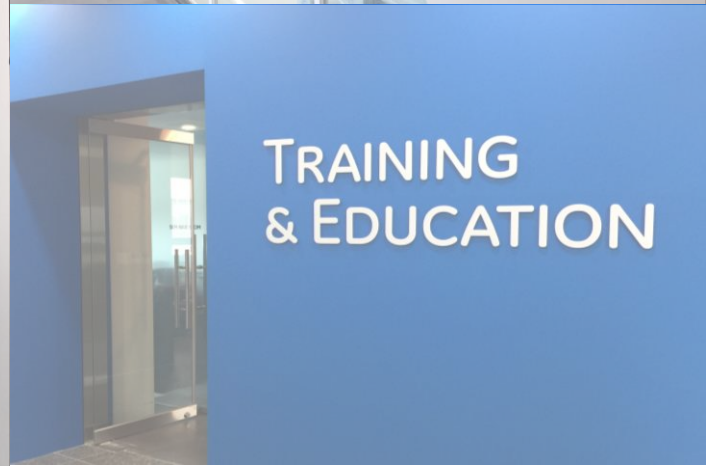
Fast Trak Center

Lab area for

Process Development

Scale-up & Pilot plant

Training & Education



Training and Process Development






Pilot scale processing

APAC Fast Trak Center Focus Area

Proof of concept (POC)

- Conversion from stainless to single-use technologies

PD offerings

- Bioreactor process development and optimization
- Resin screening and optimization
- Design of experiments (DoE)
- High-throughput process development (HTPD)
- Purification process development and optimization
- Resin cleaning in place (CIP) studies / Resin lifetime studies
- Scale up from lab scale to pilot scale

Linked to cGMP manufacturing sites

- Production of toxicology material
- cGMP BSL1 – from 10 L to 2000 L
- cGMP BSL2 – from 10 L to 500 L

Training and education courses

CELL1	Advanced bioreactor cultivation technology	Apr 18–21
DEV1	Introduction to downstream techniques and bioprocessing	May 23–25
DEV2	Downstream bioprocess development	Oct 16–20
DEV4	Bioprocess scale-up and technology transfer	Nov 29-Dec 1
COL1	Large-scale column packing	Jul 4–6
UNI1	Advanced UNICORN™ system control for chromatography systems	Sep 4–6

Our Goals

GE's Fast Trak services center is committed to:

- cultivating professionals in the industry
- solving complex process development challenges
- providing capacity for developing biologics
- bringing new expertise in developing biologics into the region




Fast Trak services

Customer case studies

1. Customer case study

Biosimilar mAb molecule conversion to single-use platform with the goal to manufacture at 2000 L scale

Customer objectives

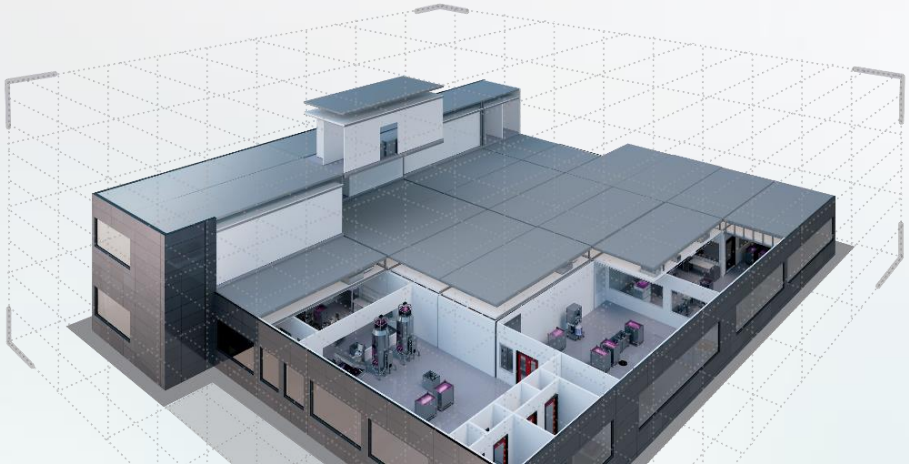
- Convert process from conventional to single-use workflow
- Scale up from 10 to 200 L. Ultimate target: 2000 L bioreactor for two mAbs
- Deploy global biosimilar manufacturing platform with aggressive timelines

Project challenges

- Molecule comparability after conversion
- Process and equipment design
- Protection of customer's intellectual property (IP)
- Communication with global teams
- Real-time scope/process changes
- Timeline challenges

Outcomes

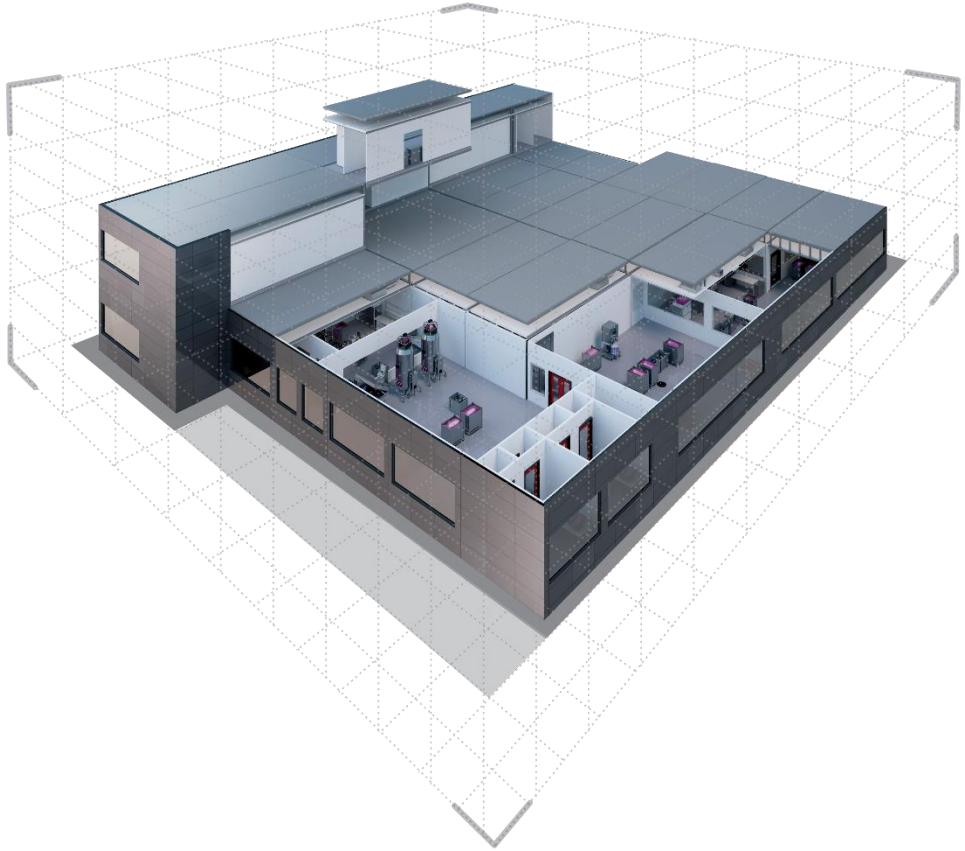
- Reduced customer development timeline by 18 months
- Developed mid-scale process in 5 months
- Transferred project to local region for further development and ultimate tech transfer to KUBio™



KUBio™ manufacturing facility

The KUBio facility is our turnkey cGMP-compliant process solution for biologics production. The modular units are factory-built, final assembly on customer site. Because different parts are developed concurrently, your KUBio facility is fully operational in just 18 to 24 months.

- Assembled on brown or greenfield site
- Built, assembled, qualified, and ready-to-run within 18 to 24 months
- Includes FlexFactory™ single-use platform
- 2 × 500 L to 4 × 2000 L facilities
- Segregated up- and downstream operations, including gowning



cGMP = current good manufacturing practices

2. Customer case study

Flavivirus production using Vero cells on microcarriers in a single-use bioreactor

Customer objectives

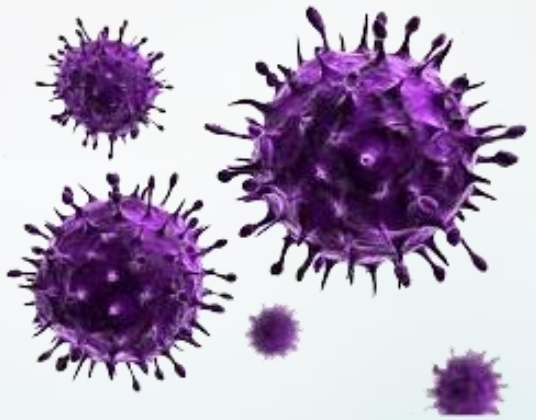
- Develop a scalable manufacturing process for inactivated whole virion flavivirus
- Compatible with single-use and conventional technologies

Project challenges

- Improve process robustness with multiple iterations
- Minimize concentrations of host cell components in harvest
- Process consistency, reproducibility, and robustness improved
- Improved process parameters for cell-to-bead attachment

Outcomes

- The process run time was reduced
- Product yield target 25%–50%
- High product purity (low residual host cell proteins and DNA)
- Material specifications meet stringent regulatory



Downstream flavivirus results

- A scalable manufacturing process for inactivated whole virion flavivirus was developed and then optimized
- Purified product yields were ~30%–45% for all generations (GENs)
- GEN2 process utilized an ultracentrifugation step, which resulted in high product purity (low residual host cell proteins and DNA)
- GEN2 and GEN3 processes resulted in the removal of the 2°C–8°C process step
- GEN3 process utilizes conventional chromatography and resulted in high product purity (the ultracentrifuge step was removed without an observed increase in residual host cell proteins and DNA)
- GEN3 process resulted in decreased processing time
- GEN3 process is compatible with single-use and conventional technologies.
- All GEN3 process materials meet stringent regulatory requirements

3. Customer case study

Scale up 293T cells and Cytodex-1 microcarrier culture to XDR50 system

Customer objectives

- Screening basal medium and FBS
- Scale up from T flask to Spinner, then to XDR 50 L. Ultimate target: 200 L bioreactor
- Deploy gene therapy manufacturing platform with aggressive timelines

Project challenges

- Attachment to microcarrier was weak
- 293T cells bead to bead transfer technics not available
- Bioreactor parameters optimization, including agitation and aeration

Outcomes

- Optimized media increased cell concentration by more than 50%
- Developed bead to bead transfer method of 293T cells
- Scaled up the process to XDR50, and future to XDR200 in FlexFactory plant

4. Application case study

Scale up Vero cells and Cytodex-1 microcarrier culture to XDR50 and XDR200 system

Objectives

- Scale up Vero cell culture process from T flask to XDR50 and XDR200
- Deploy vaccine manufacturing platform

Project challenges

- Vero cells are more difficult to detach from microcarriers
- Appropriate trypsin digestion method not available
- Vero cells bead to bead transfer process setup
- Bioreactor parameters optimization, including agitation and aeration

Outcomes

- Established Vero cells detachment method from microcarriers
- Developed bead to bead transfer method of Vero cells
- Scaled up the process to XDR50 and XDR200

5. Customer case study

Pilot-scale manufacturing non-GMP, from cell line to downstream

Customer objectives

Upstream:

- Cell line import and storage
- Medium preparation
- Seeding in WAVE Bioreactor™ system
- Cell culture in Xcellerex™ XDR-50 or XDR-200 bioreactors
- Harvest

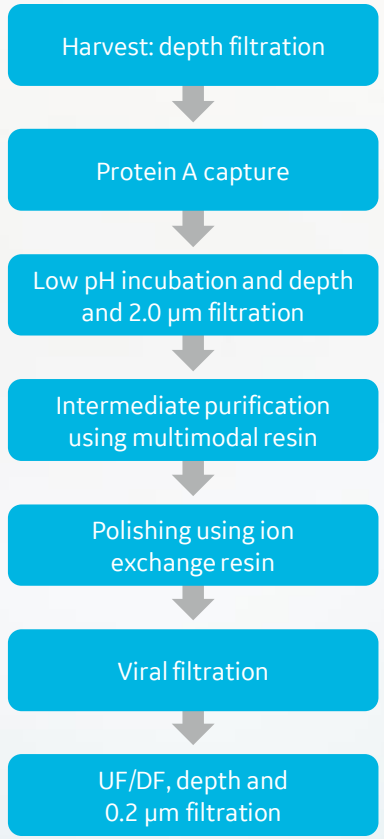
Downstream:

- Buffer preparation
- Chromatography
- Virus inactivation
- UF/DF
- Nanofiltration
- Sterile filtration

Project challenges

- Single-use or hybrid production line
- IP protection: CDA, 24 × 7 monitor, lab access

Outcomes

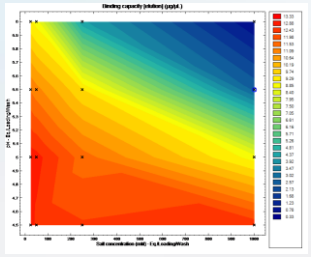


6. Customer case study

Downstream PD: Convert Phase III third generation rProtein process to a modern chromatography resin, screening via absorption isotherms and binding maps

Resin screening studies → SBC studies → Selectivity studies → DBC studies

Capto™ MMC



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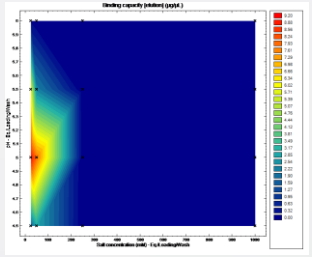
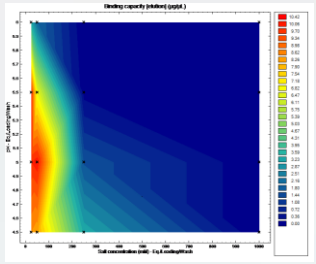
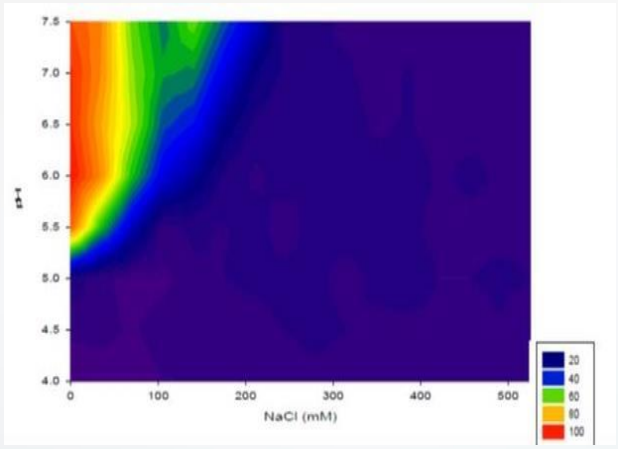


SP Sepharose™ FF



- Identified modern resin for the three chromatography steps
- Identified optimal process conditions with better flow properties

Capto DEAE



- Customer is transitioning to the modern medium

SBC = static binding capacity, DBC = dynamic binding capacity

7. Customer case study

Process optimization for biosimilar molecule for phase I – chromatography steps

Process development

- Capture step: increased DBC by 50%
- Intermediate step: simplified step, improved yield from 50% to >90%
- Polishing step: simplified step, improved yield 30% to >50% (max yield possible)
- Analytical support with Biacore™ assay
- Technology transferred to CMO

Where is the process now?

- 2000 L engineering runs
- Phase I clinical studies
- Third generation process in pipeline for phase III

8. Customer case study

Downstream process development: Resin cleaning improves the economic impact of chromatography steps by increasing the number of cycles

Resin CIP protocols

- Fouling of media in PreDictor™ plates
- Incubation of fouled media in CIP agents
- Analyzing residual impurities on the media after cleaning
- Verification of selected CIP protocol in column lifetime study

How to determine lifetime

- How many cycles are required?
  - As many as possible?
  - One campaign?
  - Only 50?

Yield of collected runs

- Cost of filling is determined by number of cycles needed
- Long lifetime resins offer 2-fold increased economic benefits due to the 2-fold increase in number of cycles

WORLDWIDE PARTNER

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www.gelifesciences.com/fasttrak

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