

Provantage® End-to-End Services Biodevelopment: from molecule to commercial production

Are you looking to expand the production of your recombinant proteins, vaccines or plasma commercial drugs? Do you need to bring affordable biosimilars to emerging markets?

Provantage® End-to-End Services encompass the support and expertise you need to accelerate clinical drug development, scale your process and implement local production facilities, globally.

Whether you are looking to implement proven solutions while reducing costs and mitigating risk, or looking for a partner who will work with you from Process Development through Facility Design and Construction anywhere in the world, we have options that will streamline your process and set you on the path to success.



Process Development

Process Development Services

- Cell line development
- Clone selection
- Media & feed screening
- Upstream Process Development
- Master Cell Bank establishment
- Downstream Process Development
- Formulation Development
- Analytical methods development & optimization
- Analytical Process Development support
- Biosimilars comparability analytical programs

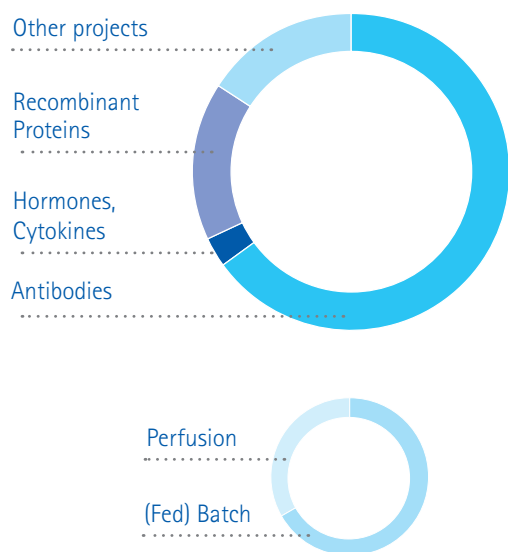


PROVANTAGE® END-TO-END SERVICES

Defining and achieving success criteria for your project

From the start of your project, you will have access to a dedicated, experienced team of Process Development and Biologics Production experts led by a knowledgeable Project Manager. From process development to GMP clinical supply, process design, facility design and construction, tech transfer and training, and operational launch, your multidisciplinary team will work with you, delivering optimal results and guaranteeing your success. Through regularly scheduled meetings, your Project Manager will ensure your expectations and milestones are met, focusing on scope, time, financial management, risk mitigation strategy and quality.

Full expertise in protein development, demonstrated through more than 200 projects



Martillac – FRANCE

Mammalian cell based Upstream and Downstream process development and cGMP production facility



Billerica, MA – USA

Mammalian cell based Upstream process development center

Provantage[®] ClinicReady Template

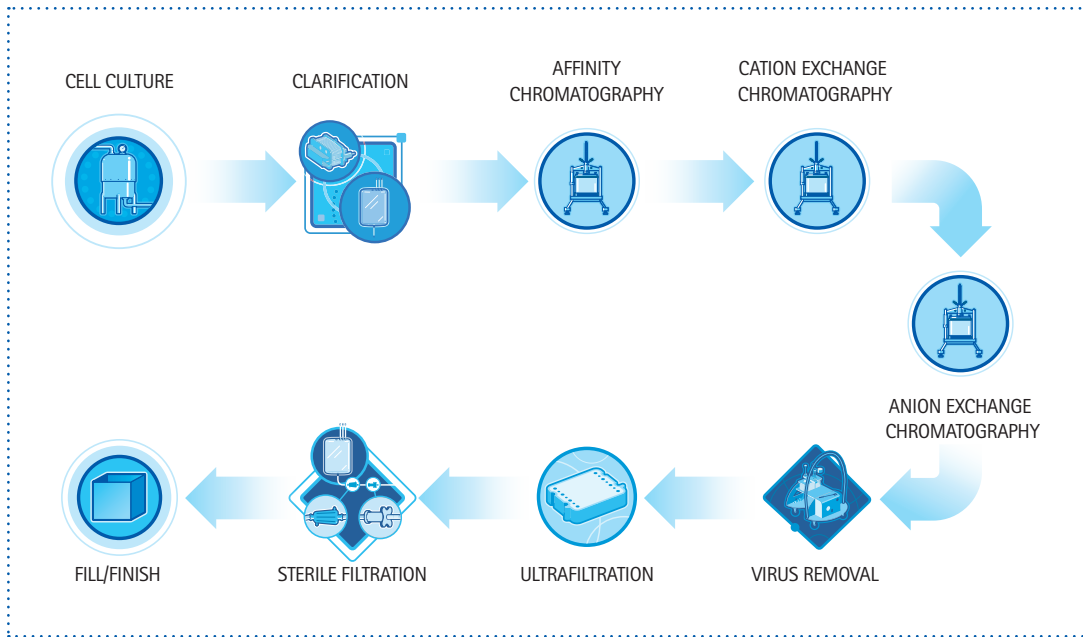
Accelerate Process Development with a Clinical Scale Template

Developing and implementing a clinical scale process can be time consuming and complex, requiring specification, sourcing and integration of many components.

To reduce time and complexity, established drug manufacturers will use process templates developed and optimized from experience with previous molecules.



PROVANTAGE[®] END-TO-END SERVICES



**Provantage®
ClinicReady Process**

Single use process template for GMP clinical scale production of monoclonal antibodies



Provantage® ClinicReady Production Template for MABs will provide you with:

- Configurable Upstream and Downstream single-use production equipment for MABs adapted to cGMP production of pre-clinical, Phase I, II and III material.
- Complete understanding and knowledge of the performances of our technologies used in the template, guaranteeing process robustness and efficiency.
- Standardized unit operations and operating parameters, standardized buffers, easier tech transfer.
- Adaptable specifications for each project, with integration of competitive products and technologies as required.

GMP Clinical Supply Solutions

State-of-the-art GMP production capabilities

- Production of mAbs, Fc-Fusion proteins, recombinant proteins, hormones

- **Track record of GMP batches released**

- **MAbs: 46 GMP batches manufactured – 150 L to 2000 L***
- **Fc-Fusion: 75 GMP batches manufactured – 150 L to 2000 L***

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- Full single-use Upstream and Downstream suites

- Cell culture: 2x 50 L single-use
 4x 200 L single-use
 2x 2000 L single-use*

- QA support for product release and CMC documentation
- French Health Authority (ANSM) approved for cGMP related activities; Internal Quality Standards equivalent to Merck Serono, the biopharmaceutical business of Merck, KGaA, Darmstadt Germany standards

Open Source Manufacturing

When the time comes to scale up your production process, transfer it to a local manufacturing partner for routine production, or move it and build your own facility, we will work with you to ease the process and make your program a success. You will have access to state of the art GMP production capabilities with full freedom and transparency needed to design your upcoming production strategy.

- No royalties
- Transparent data and knowledge transfer
- Freedom to transfer your process anytime, anywhere

*2K Liter GMP production in 2015

Available from 3L through 2000 Liter, Mobius® bioreactors have been designed to ensure that ease-of-use and operational flexibility at small scale can be translated to full scale production.



Tech Transfer

If you are looking to tech transfer your existing Vaccine, Plasma or Recombinant Protein production process into a new facility, we have the products, services and partnerships you need to be successful.

Tech Transfer Services

- Full facility design and engineering
- Process design
- Facility build up
- Specification and supply of your upstream and downstream equipment platforms
- Equipment qualification
- Process technical transfer
- Facility start up and operation

Implementing Single-Use Technologies

The many economic advantages of single-use technologies are well known, leading to increased adoption in biopharmaceutical processes. Faster process turnaround with reduced cleaning cycles, increased flexibility with possibility to scale up volume easily, or run multi products using the same equipment within the same production space, are driving single-use implementation.

However, implementation of single use technologies across the process should be carefully risk assessed so that expected advantages such as resources savings, higher production uptime or lower cleanroom classification needs are not inhibited by batch losses or production downtime issues.



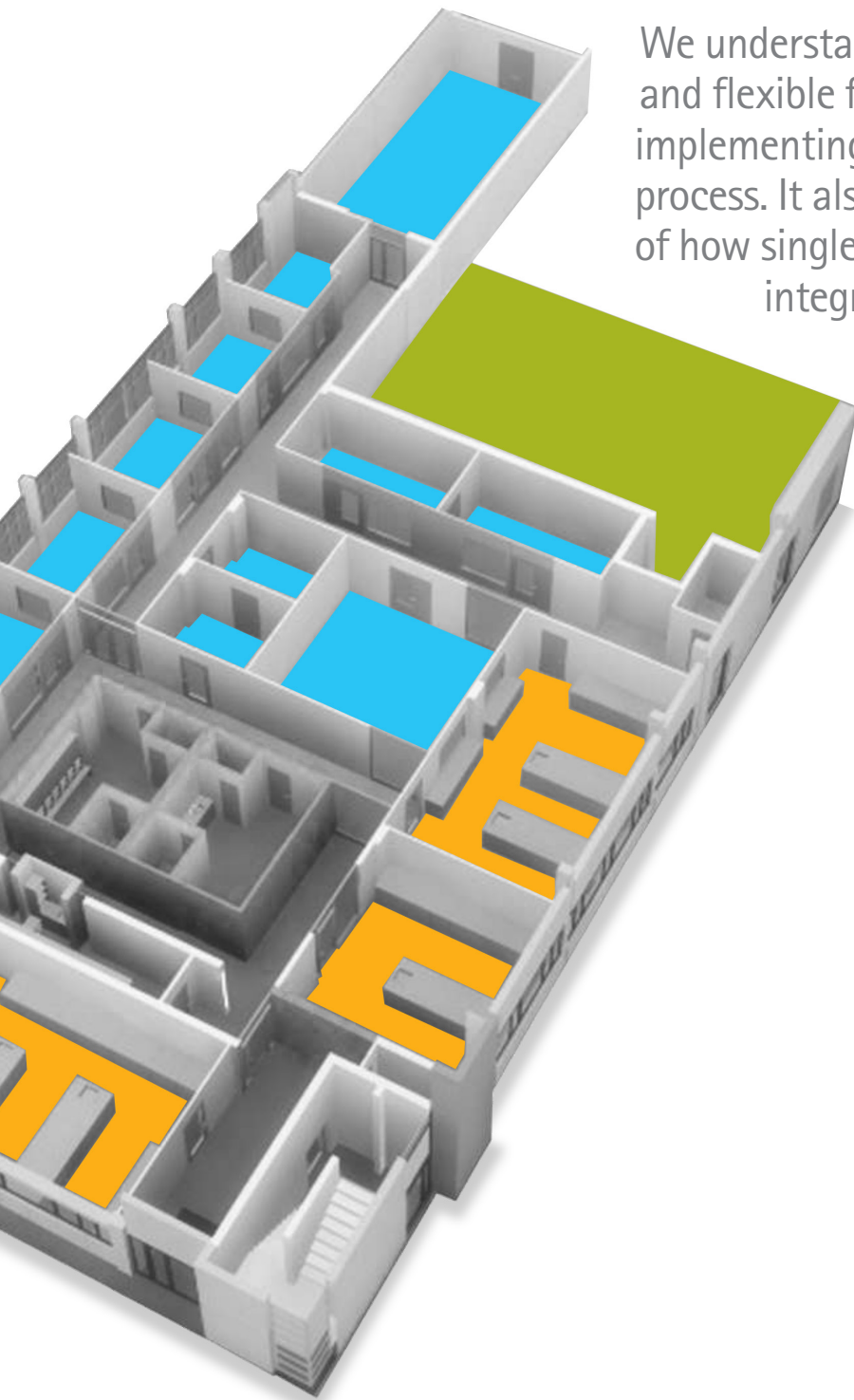
Your production train, where and when you need it.

Our hardware engineering team will create a system design and automation solution tailored to meet your needs. Having supplied hundreds of single-use, multi-use or hybrid systems to biopharmaceutical industry for more than 50 years, you will benefit from our extensive expertise and know-how.

We also recognize that our product portfolio does not cover all unit operations from customer's processes. For unit operations not part of our core business, we will partner with technology suppliers, integrating outside solutions into your processes.



Facility Design and Construction



We understand that building agile and flexible factories is not only about implementing a single-use production process. It also requires careful consideration of how single-use processes will be integrated into a facility designed and built to get the best outputs to meet your unique needs.

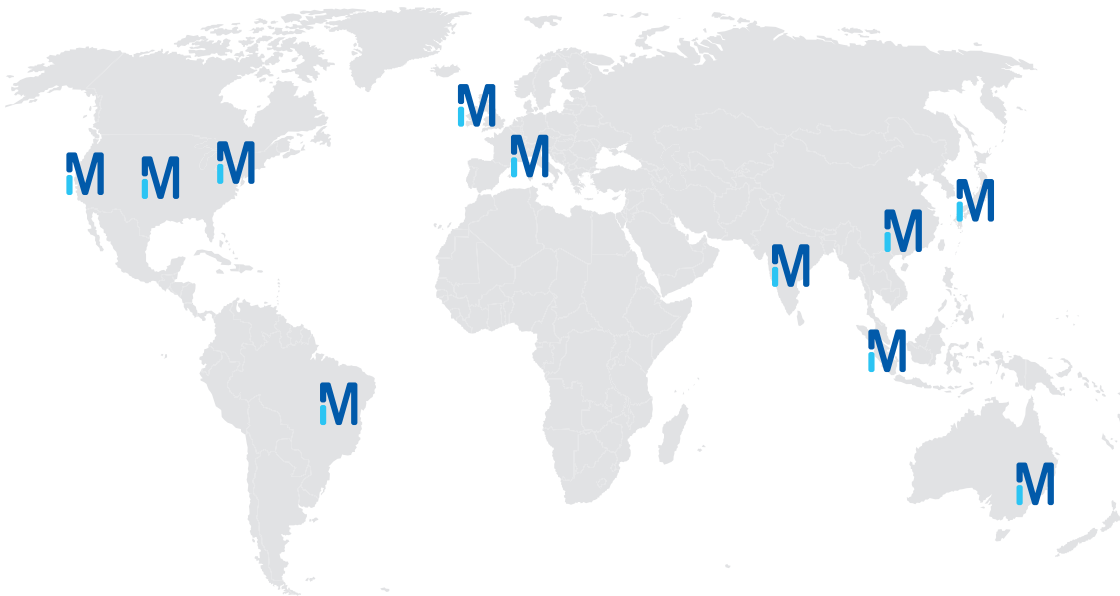
Working closely with leading modular cleanrooms, facility engineering and construction companies, we will work with your team to find the right solution and bring your project to life.

Once your facility is ready, process technical transfer activities can happen, ensuring process reproducibility and validating the capacity of your site to run your process.

Our local team of experts will work with you to develop and execute the process technical transfer plan including tech transfer protocol, associated tests and reports, raw materials and consumables required, as well as a detailed process description, process risk analysis and training plan for your upstream and downstream production technicians and operators.

Local Support, Globally

Local field services engineers will ensure reception of your equipment at your production site. They will then execute site acceptance test, installation and operational qualification (SAT, IQ/OQ) in compliance with cGMP regulations. They will also ensure maintenance services to guarantee optimal performance of your equipment over time.



Provantage® End-to-End Global Network

Our global network is comprised of approximately 80 process scientists and engineers, providing a wealth of experience and vital technical support in areas such as:

- Equipment installation and qualification
- Local operator training programs
- Technical troubleshooting on site
- Design of custom recipes to specifically adapt your equipment to your process
- Performance Qualification (PQ) of your process with targeted advice during equipment preparation, dry run of your process recipe, or real qualification runs
- Equipment Maintenance Services



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To Place an Order or Receive Technical Assistance

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France: 0825 045 645

Germany: 01805 045 645

Italy: 848 845 645

Spain: 901 516 645 Option 1

Switzerland: 0848 645 645

United Kingdom: 0870 900 4645

For other countries across Europe,
please call: +44 (0) 115 943 0840

Or visit: www.merckmillipore.com/offices

For Technical Service visit:

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