MERCK

TAKE THE RIGHT PATH UPSTREAM

Products and Services for mAb Upstream Development

Millipore®
Preparation, Separation, Filtration & Monitoring Products

SAFC®
Pharma & Biopharma Raw Material Solutions

BioReliance®
Pharma & Biopharma Manufacturing & Testing Services

The life science business of Merck operates as MilliporeSigma in the U.S. and Canada.

Merck has brought together the world's leading Life Science brands, so whatever your life science problem, you can benefit from our expert products and services.

Millipore®

Preparation, Separation, Filtration & Monitoring Products

The Millipore® portfolio of Merck offers an ecosystem of industry-leading products and services, spanning preparation, separation, filtration and monitoring – all of which are deeply rooted in quality, reliability and timetested processes. Our proven products, regulatory and application expertise are a strong foundation you can rely on to consistently perform at the highest level.

SAFC®

Pharma & Biopharma Raw Material Solutions

The SAFC® portfolio of Merck offers customized and ready-to-use raw material solutions, backed by deep regulatory expertise. Our high-quality products and services are supported by an experienced and responsive team of raw material and regulatory experts who are committed to understand your requirements and provide tailored solutions that meet your exact needs.

BioReliance®

Pharma & Biopharma Manufacturing & Testing Services

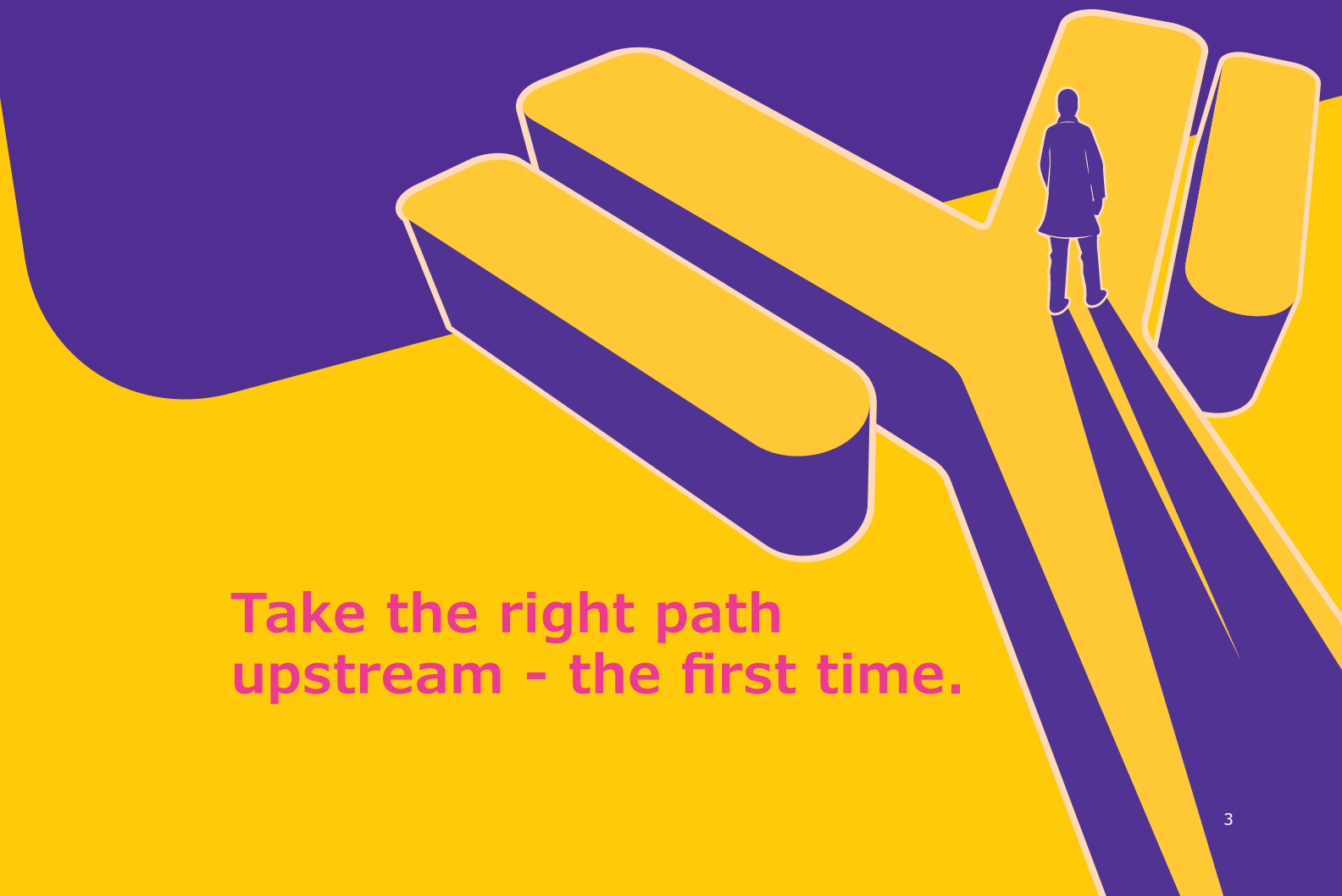
The BioReliance® portfolio of Merck encompasses biopharmaceutical characterization, safety testing and process development, as well as clinical and commercial biomanufacturing. Our experienced teams and operational expertise make us the partner who supports you all the way and always has your vital goal in mind.

Table of Contents

When developing a monoclonal antibody with a world of potential, getting your upstream process development right the first time opens up exponential possibilities.

The decisions you make in upstream development have major impacts on your process performance. Wrong decisions are difficult to reverse or require significant backtracking and resources. Yet, all these critical decisions need to be made amid the race to market.

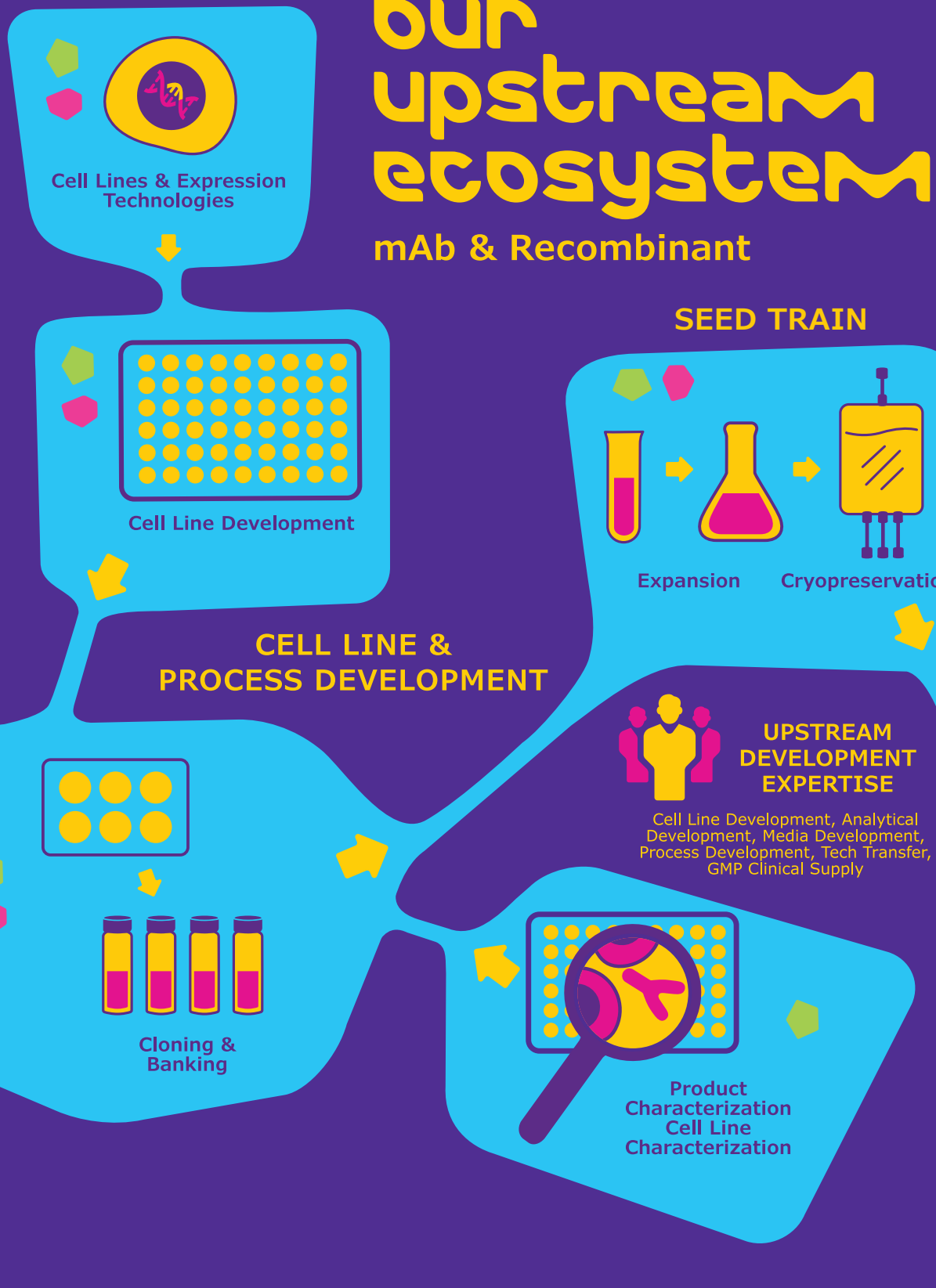
Our upstream ecosystem - comprised of cell line and media platforms, cell line development, product characterization services, bioreactors, single-use mixers, process development expertise and next generation processing programs - gets upstream process development right the first time. You save precious time, optimize performance, improve feasibility and sustainability, while laying the groundwork for downstream success.



Take the right path upstream - the first time.

our upstream ecosystem

mAb & Recombinant



BioReliance® Services

SAFC® Products

Millipore® Products

MerckMillipore.com/right-path-upstream

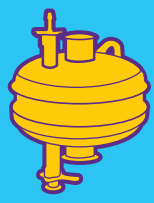
MEDIA DEVELOPMENT

Biopharma Raw Materials & Supplements

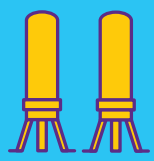
Custom Media

Catalog Media ("Fed Batch" and "Perfusion" Media)

Media Mixing

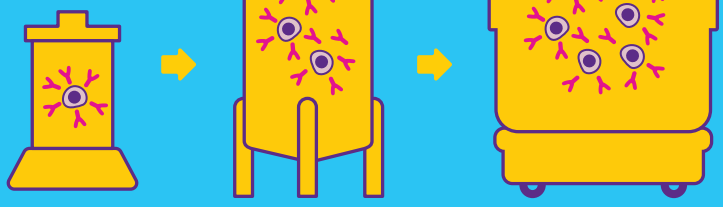


Virus Filtration



Sterile Filtration

PRODUCTION



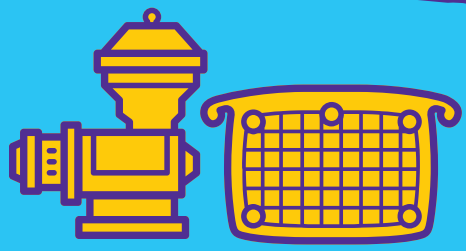
Bioreactor (Fed Batch or Perfusion Mode)

Raw Material Testing

ANALYTICS & BIOSAFETY

Sensors & Software

Lot Release Testing Product Characterization



Clarification

Cell Lines

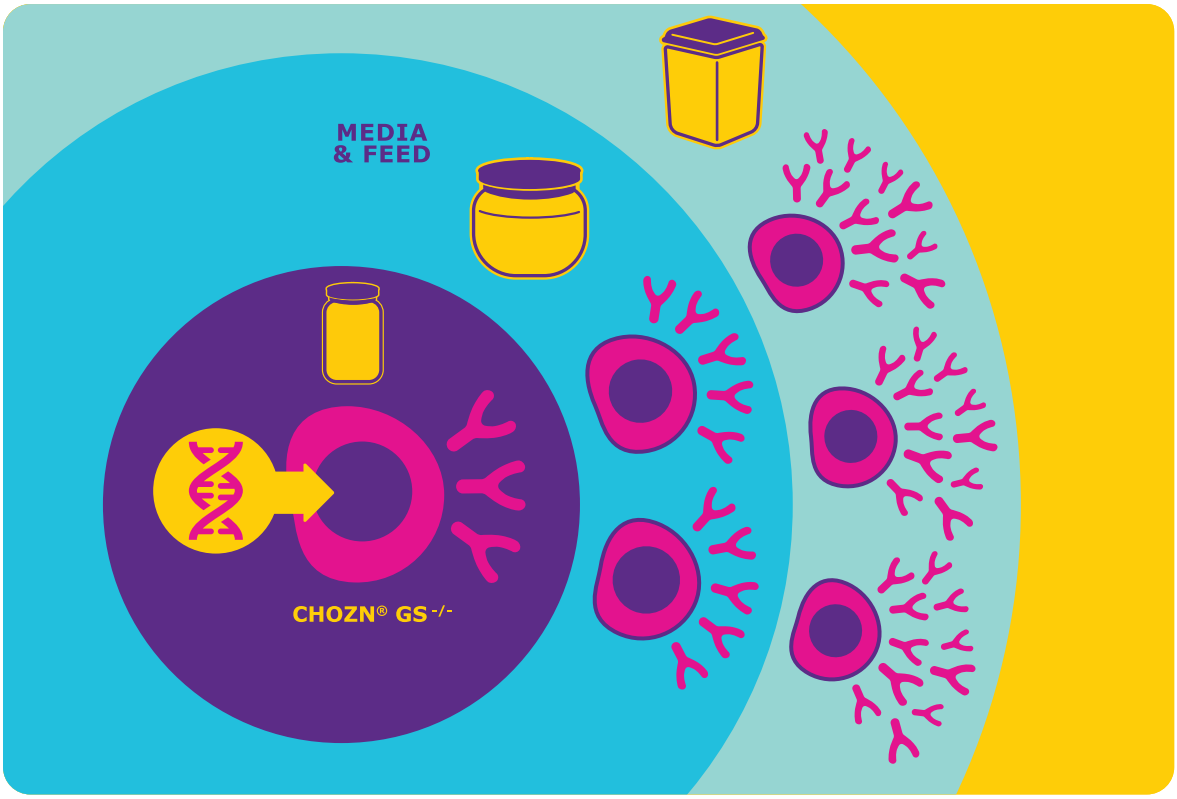
CHOZN® Expression Platform

The CHOZN® platform is a mammalian cell expression system based on CHO cells (Chinese Hamster Ovary) for fast and easy selection and scale up of stable clones producing high levels of recombinant proteins.

The CHOZN® platform is:

- Highly productive
- Highly robust and stable
- Proven scalability
- cGMP cell banked
- Paired with optimized media & feeds

In addition, the CHOZN® platform provides complete cell line traceability documentation and trusted technical support.

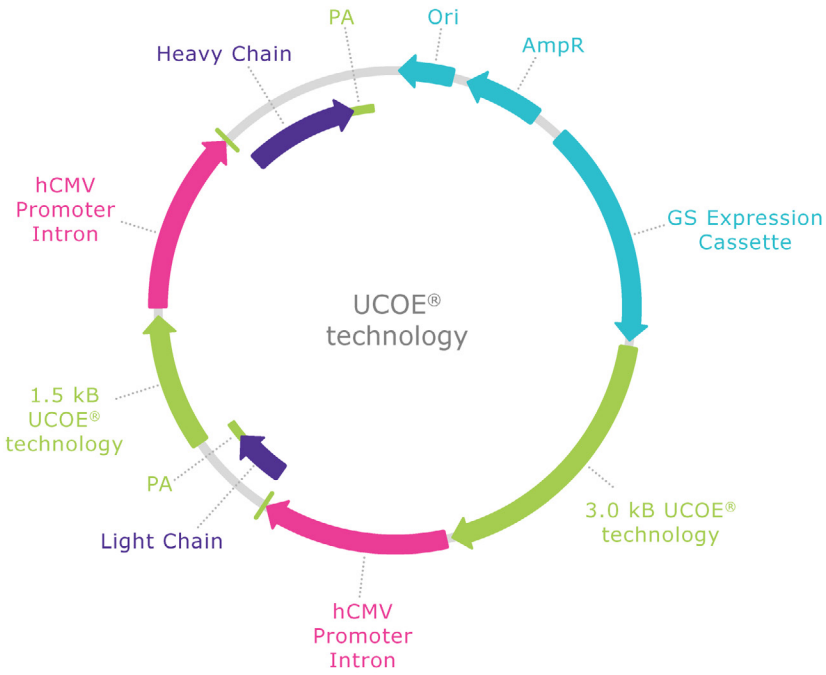


SAFC®

Pharma & Biopharma Raw Material Solutions

The CHOZN® & UCOE® Combined Platform

The CHOZN® & UCOE® Combined Platform streamlines processes and offers numerous efficiencies for cell line development.



The CHOZN® & UCOE® Combined Platform expands on the benefits of the CHOZN® GS expression system by:

- Accelerating cell line development through increased efficiency of isolating 8-fold more high producing clone candidate pools
- Increasing cell line development success with hard-to-produce molecules
- Achieving high and stable titers to expedite cGMP manufacturing with fewer resources

Cell Lines

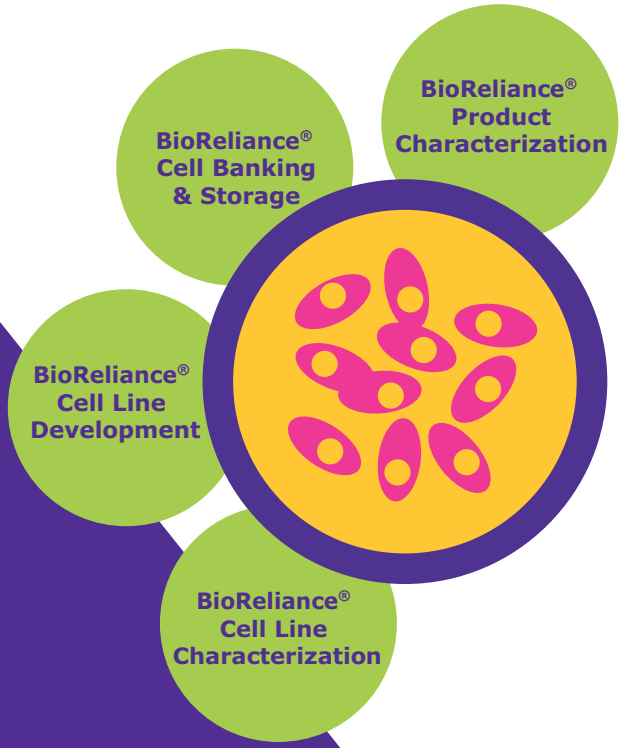
Cell Line Characterization

Cell Line Characterization is required by the regulatory bodies to ascertain that the cell line is of the expected identity (both the species of origin and the transgene) and free of adventitious agents.

When generating biopharmaceuticals, extensive cell line characterization assays are required for mammalian and non-mammalian cell lines at various stages of drug production.

We recommend checking:

- Identity – test to confirm the species of the origin
- Purity – test for the presence of adventitious agents
- Genetic stability – test the integrity of the transgene and the production cells



Cell Banking

Our cGMP production facilities allow our experts to produce your Master Cell Bank (MCB) and Working Cell Bank (WCB). Your MCB is critical to therapeutic product development and supports not only clinical development and manufacturing but also the commercial supply phase for biologicals. A WCB is produced from a single vial of the MCB that has been grown for several passages and cryopreserved for later stages of therapeutic development and manufacturing.

BioRepository

Safe sample storage is our priority. We have a segregated, GMP-compliant (21CFR610), storage facility for your samples across our three sites which mitigates the risk of interrupting your manufacturing operations through split site storage.

Lot Release Testing Services

Every batch of biologic produced must undergo lot release testing to comply with comprehensive regulatory guidance on quality and safety. This includes detailed analysis of not only the raw materials, but also the bulk harvest, purified bulk (drug substance) and the final filled product (drug product).

We support lot release testing at any stage of the biomanufacturing process including adventitious agent detection, identity, purity, potency, and residuals and excipients testing.

BioReliance®

Pharma & Biopharma
Manufacturing &
Testing Services

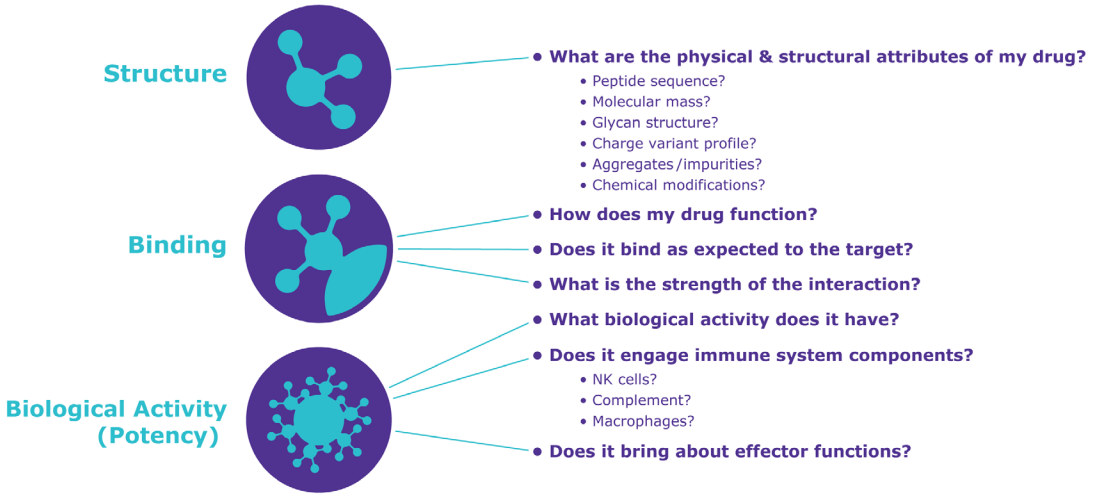
Product Characterization

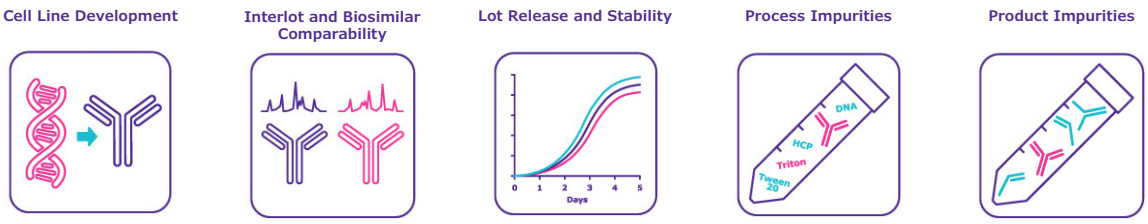
Our comprehensive program reveals the true identity of your molecule through every phase of development, ensuring your biotherapy's safety, purity, and potency. You can select from one of our mAb-based assay packages or a custom assay tailored to your biologic.

Pre-configured, off-the-shelf packages designed to speed time to actionable data

Establish your drug's quality attributes (product characterization) empirically by physical, structural, binding, and functional analysis, at early phase of drug development

Analytics and characterization answer crucial questions





BioReliance®

Pharma & Biopharma Manufacturing & Testing Services

Media Development

4CHO Fed-batch Media and Feeds

Cell culture media are important for process efficiency and mAb quality. Production media support initial cell growth and production, while the feed replenish depleted nutrients required for cellular function and maintain and extend the production phase in fed-batch mode.

EX-CELL® Advanced and Cellvento® 4CHO platform media and feeds support growth and productivity across a diverse set of CHO cells in fed-batch cultures. The high concentrated feed allows a reduction of the added feed volume thereby increasing the volumetric productivity.

- Chemically defined
- Consistent cell growth and performance
- Available in powder or compacted format
- Robust scalability

SAFC®

Pharma & Biopharma Raw Material Solutions

Media Development

BioPharm Materials Ingredients and Supplements

Our comprehensive portfolio of cell culture ingredients, non-animal origin and animal-derived cell culture supplements can help you stabilize your processes and obtain optimal yields with consistent results.

Modified amino acids

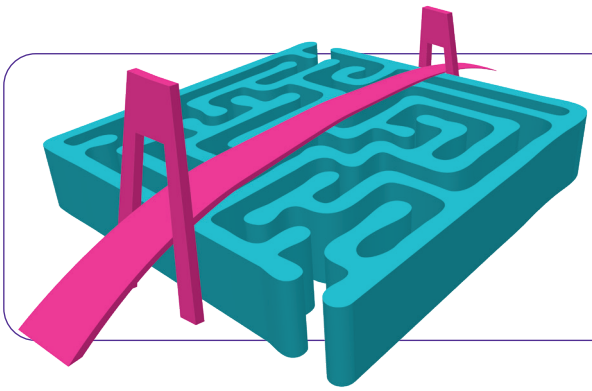
Phospho-L-Tyrosine disodium salt and S-Sulfocysteine sodium salt can be used at neutral pH, replacing the need for an alkaline feed.

Non-animal origin supplements

Formulated for cell culture applications, recombinant manufacturing ensures reliable supply and outstanding lot-to-lot consistency.

EX-CYTE® supplement

A water-soluble concentrate of cholesterol, lipoproteins and fatty acids, to enhance cell growth and protein production for your mammalian cells.



Poloxamer 188 Emprove® Expert

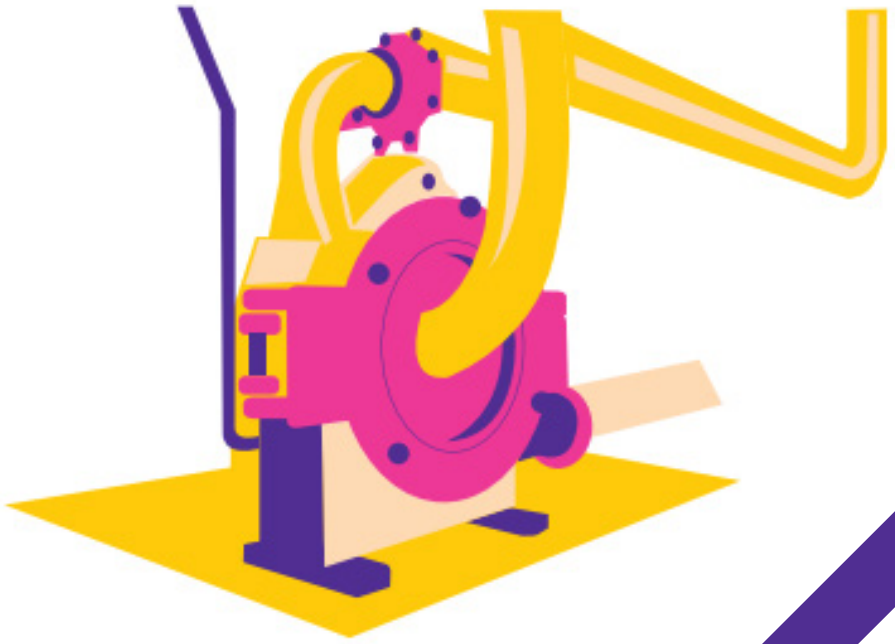
Poloxamer 188 Emprove® Expert is a surface-active nonionic polymer used in cell culture media as a shear protectant. It was demonstrated to increase the robustness of mammalian cells to shear from sparging.

Media Development Services

Our team of scientists are experts in developing custom media formulations resulting in optimal cell culture performance. The science we use to make our own proprietary formulations can be applied to improve the performance of your unique clone or media platform.

ImMEDIAte ADVANTAGE® Small Volume Custom Media

Our ability to support and be your partner for bioprocess development activities is strengthened by more than 40 years of cell culture media formulation and manufacturing expertise. Our imMEDIAte ADVANTAGE® service for pre-GMP, small scale custom media, feeds, supplements and buffers provide quick turn-around service giving you the competitive advantage to complete your development work quicker and accelerate your molecule to market sooner.



SAFC®

Pharma & Biopharma Raw Material Solutions

Media Development

Custom Media

Whether producing our own proprietary formulations or yours, our proven ability to manufacture high quality, fit-for-purpose, industrial cell culture media in a multi-facility approach provides the global supply continuity you need.

You can rely on our experience and expertise in raw material supply security, industry-leading manufacturing technology, and quality testing and documentation for liquid or dry powder formulations.

Bulk Powder Transfer Bags

Our EZ BioPac® transfer bags and Right Sized Weighing offer provides you with the safest and most convenient way to directly add our products to your hydration vessel. By eliminating the need to reweigh, this complete solution protects your operators and facility from unnecessary exposure to dust, saving time and increasing efficiency.

SAFC®

Pharma & Biopharma Raw Material Solutions

Single-use Bioreactors and Mixers

Mobius® Single-use Bioreactor

Mobius® Bioreactors are a scalable portfolio of stirred tank bioreactors that provide flexibility by configuring software, hardware and single-use assemblies for use in fed batch and perfusion cell culture applications.

Our bioreactor platform has been designed to ensure that ease-of-use and operational flexibility at small scale can be translated to full scale production.

Mobius® Power MIX

The Mobius® Power MIX single-use mixing systems combine high performance mixing technology with design features that make them easy-to-use and are available in capacities from 50 L to 3000 L. The impeller design and motor are based on our magnetically coupled NovAseptic® mixing technology, a proven mixing technology in stainless steel tanks. These systems efficiently mix the most challenging buffers, media and biopharmaceutical ingredients.

Millipore®

Preparation, Separation,
Filtration & Monitoring Products

Biosafety

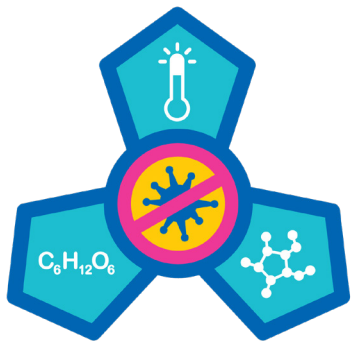
Viresolve® Barrier Filters

Specifically designed to process cell culture media, Viresolve® Barrier filters are the last line of defense against bioreactor contamination. These filters have demonstrated high retention of virus, mycoplasma and bacteria, including spirochetes, while providing high flow and capacity.

HTST Treatment

Our high temperature, short time (HTST) technology offers a reliable option for viral inactivation of high risk raw materials. Through precise control of temperature and residence time, HTST treatment has been shown to achieve approximately 6 log virus reduction.

HTST treated glucose (and other sugars) is available for both clinical and commercial scale operations.

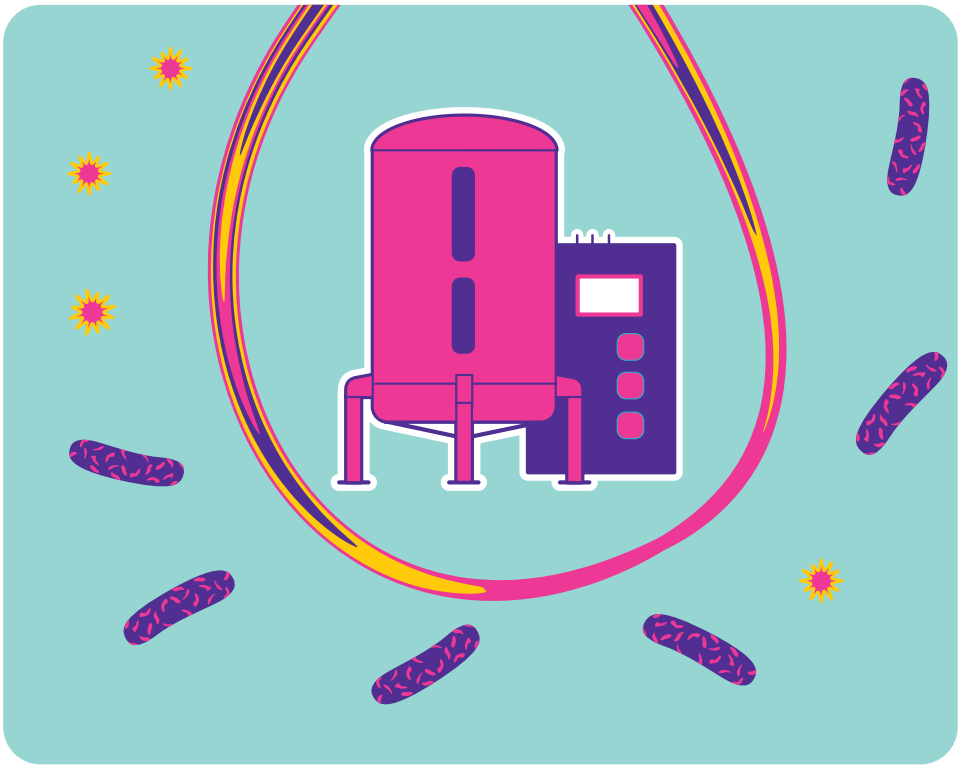


Millipore®

Preparation, Separation,
Filtration & Monitoring Products

Sterile Filtration

To reduce the risk of bioreactor contamination, cell culture media is often processed through sterilizing filters. Our sterilizing-grade filters contain our trusted Durapore® or Millipore Express® membranes with different microbial retention specifications to meet your individual process needs.



17

Seed Train & Perfusion

Cellvento® 4CHO-X Expansion Medium

Reducing the number of bioreactors in the seed train leads to better facility utilization and eliminates traditional bottlenecks. Using N-1 perfusion enables the inoculation of a production bioreactor with higher cell densities for high seed production process formats.

Cellvento® 4CHO-X Expansion Medium has been developed for N-1 perfusion for CHO cell lines. It is formulated with a high nutrient concentration to achieve low cell specific perfusion rates (CSPRs) at high cell densities.

EX-CELL® Advanced HD Perfusion Medium

Next generation perfusion processes require a new type of medium to facilitate high productivity at low perfusion rates.

EX-CELL® Advanced HD Perfusion Medium was designed for CHO cells to reach and maintain high cell densities at low cell specific perfusion rates (CSPRs), while supporting high volumetric productivities of monoclonal antibodies and recombinant proteins in suspension culture.

SAFC®

Pharma & Biopharma Raw Material Solutions

Seed Train & Perfusion

Cellicon™ Perfusion Filter and Controller

The benchtop Cellicon™ Perfusion Solution is designed to meet your perfused seed train challenges. It consists of a controller and a flat sheet cell retention filter running in tangential flow filtration mode built in a single-use assembly.

This easy-to-use solution increases perfusion process efficiency, provides real-time monitoring and control for reliable and consistent performance.

Millipore®

Preparation, Separation,
Filtration & Monitoring Products

BioReliance® Validation Services

Accelerate and simplify your path to patients by letting our experts help you choose and conduct the appropriate validation services for your filters, assemblies and single-use systems.

Trust our global services network for:

- Chemical compatibility for filters and single-use technologies
- Integrity testing
- Extractables and leachables studies
- Patient safety evaluation
- Regulatory consultancy and custom study design

BioReliance®

Pharma & Biopharma
Manufacturing &
Testing Services

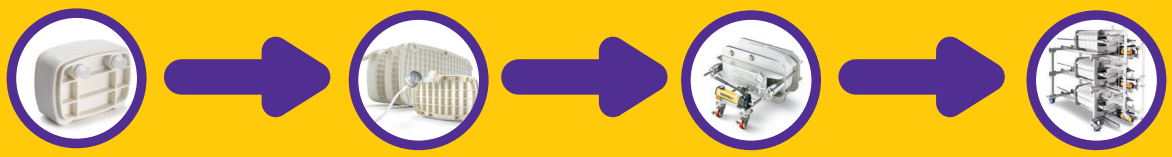
Clarification

Millistak+® Filters

With more than 40 years of clarification experience, we are committed to introducing innovative, easy-to-use technologies, like Millistak+® Pod and Clarisolve® disposable depth filters, to help improve your productivity and process efficiency.

Unparalleled Scalability

The Pod holder system's modular design makes it easy to configure a system for a specific application and conveniently reconfigure it as process capacity requirements scale-up or down. The flexible, modular format offers scalability from 5 up to 20,000 liters or more.



Small Scale | Lab Scale | Pilot Scale | Process Scale

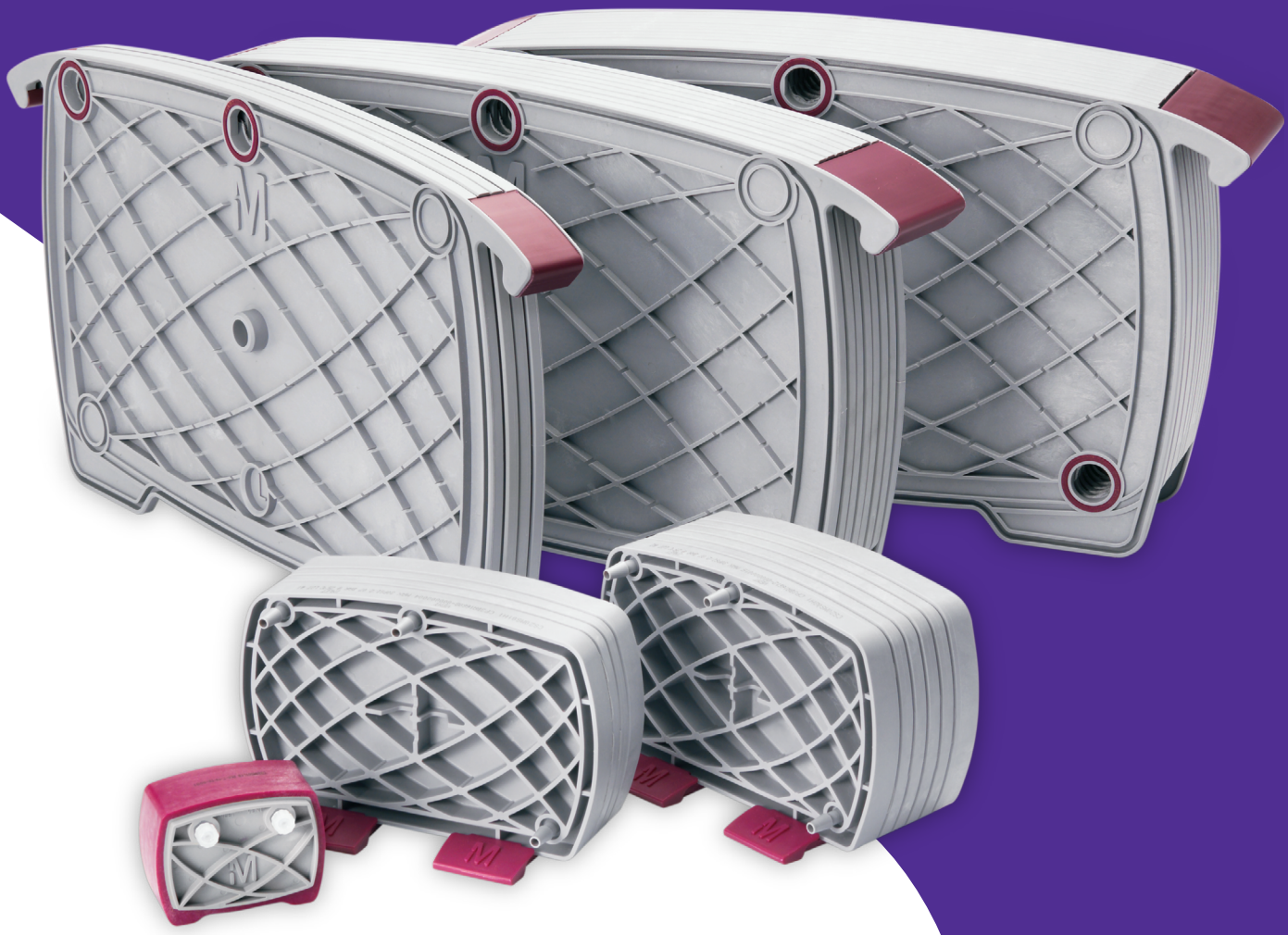
Millistak+® Pod Disposable Depth Filters

Millistak+® CE, DE, and HC Pod is ideally suited for primary and secondary clarification. These disposable depth filters offer flexibility and ease of use through their unique modular design.

- Compact design maximizes product yield and minimizes facility footprint
- Scalable from 5 L up to 20,000 L
- Disposable pod device protects operators from exposure to biohazards and eliminates the cost of housings, Cleaning in Place (CIP) and cleaning validation

Millipore®

Preparation, Separation,
Filtration & Monitoring Products



Millistak+® HC Pro Synthetic Depth Filters

Millistak+® HC Pro fully synthetic depth filters provide a cleaner and more consistent depth filtration media as compared to current diatomaceous earth (DE) and cellulose (CE) based filter media.

- Reduced TOC extractables and a 50% reduction in the recommended pre-use flush volumes
- No beta-glucans to interfere with Limulus amebocyte lysate (LAL) testing for bacterial endotoxins
- Improved lot-to-lot consistency
- Provides as much as two times the filtration capacity with equivalent filter retention over commercial DE-based benchmarks for primary clarification
- Improved HCP impurity clearance

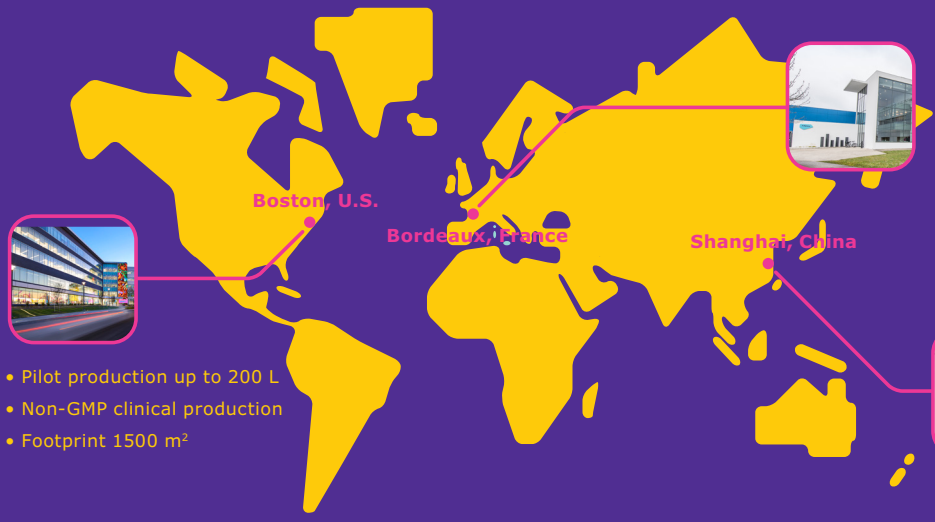
BioReliance® End-To-End Solutions

Contract Development and Manufacturing Services

Adaptability. At Every Stage.

We are a contract development and manufacturing organization within one of the largest science and technology companies in the world. We bring a wealth of in-house expertise and leverage our bioprocessing technologies, offering integrated packages from cell line development and process development to GMP manufacturing. Our clients include early-stage and small biotech companies. We offer a flexible approach to balancing cost, risk and speed to clinic, utilizing our 33+ years of experience that helps you make informed decisions. When you work with our BioReliance® End-to-End Solutions team, you have access to all our services, regulatory expertise and our latest Single-Use technologies – all without upfront payment or booking fees, while having a dedicated project manager.

A Global Network of Biodevelopment Centers



- Pilot production up to 200 L
- Non-GMP clinical production
- Footprint 1500 m²

- Fully single-use manufacturing capabilities
- Pilot production up to 200 L
- GMP clinical production up to 4,000 L
- GMP commercial production planned for 2020
- 8 single-use Mobius® bioreactors
- Footprint 41000 m2
- 3 manufacturing suites

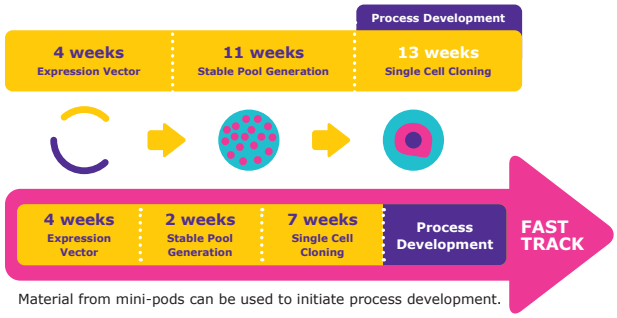
- Pilot production up to 200 L
- Non-GMP clinical production
- GMP clinical production planned for 2020
- Footprint 5150 m2

Our Experts Implement Custom Solutions from DNA to Market

Plug & Play Upstream Development Service

Get Easy Access to a Tailored Suite of Services

Take advantage of our mini-pool approach to speed up development by up to 13 weeks



Material from mini-pods can be used to initiate process development.

Add-on services give you options to choose the path that's right for you:

- Off-the-shelf Media & Feed Screening
- Analytical Method Development
- Complete Analytics
- GMP Master Cell Bank & Cell Bank Characterization
- MCB Storage

Support for all phases of drug development

Service	Preclinical	Phase I	Phase II	Phase III	Commercial
Cell banking & testing	•	•	•	•	•
Raw materials testing	•	•	•	•	•
Lot release testing	•	•	•	•	•
Clearance validation		•		•	
Virus manufacturing	•	•	•	•	•

BioReliance® cell banking services provide cGMP manufacturing of mammalian master and working cell banks.

Cell Line Characterization services:

Cell line characterization is the process of evaluating the identity, purity and genetic stability of the cell line. Recognized as a global leader in biosafety testing, we have proven expertise in every aspect of cell line characterization. Operating from global, world-class facilities — staffed by highly trained personnel and equipped with the very latest technologies — we offer a full range of identity, purity and genetic stability testing services.

BioReliance®

Pharma & Biopharma Manufacturing & Testing Services

The Advanced Emprove® Program

The Emprove® Program. Your fast track through regulatory challenges

Ensuring the compliance of your pharma and biopharma products involves the compilation of a vast amount of data, which can be time- and resource-intensive. In order to facilitate and accelerate this process we developed our Emprove® Program. It includes more than 400 pharma raw and starting materials and a selection of filtration and single-use products. Each product in the portfolio is complemented with three different types of dossiers supporting you throughout the different stages of your operations: qualification, risk assessment, and process optimization, speeding your way through the regulatory maze.

The Emprove® Program simplifies your processes by:

- Accelerating approval preparation
- Facilitating qualification processes
- Supporting risk assessment, management and mitigation
- Increasing supply chain transparency
- Saving time and money

When using raw and starting materials including excipients, risk levels vary depending on the product manufactured and its application. The different categories provide exactly the information for the products used as per the end user's needs.

EMPROVE® EVOLVE

Product line provides fit-for-purpose high quality raw materials designed for the earlier stages of regulated manufacturing processes along with detailed and transparent supply chain information and documentation to support risk assessments.

EMPROVE® ESSENTIAL

Product line is designed for moderate risk levels. Best-in-class regulatory support is combined with our high quality standards.

EMPROVE® EXPERT

Product line addresses higher risk applications, where the lowest microbiological and endotoxin levels are of utmost importance. These products are documented as being manufactured with low microbio logical and endotoxin levels.

EMPROVE® API

Product line provides the right quality and regulatory documentation required for active pharmaceutical ingredients. All the products in this line are manufactured in Europe and comply with ICH Q7 requirements.

Emprove® Program for Filtration and Single-Use

Due to the need of high transparency and standardization across the whole supply chain, the Emprove® Program also includes filtration and single use technologies ranging from sterile, clarification and virus filters to single-use components used in the major steps of the biopharmaceutical process.

Extractables data summarized as per BioPhorum's standard testing protocol and USP <665> form a part of the dossiers to support safety risk assessment seamlessly.

The three different types of dossiers support you throughout the different stages of your operations:

Material Qualification Dossier

Information to start material qualification.

Quality Management Dossier

Answers questions during risk assessment.

Operational Excellence Dossier

Supports process optimization

Comprehensive regulatory information at your fingertips

The Emprove® Suite is your online gateway to conveniently access all our Emprove® dossiers on demand.

The Emprove® Suite is always up-to-date and optimized for any targeted search. While the material qualification dossier is available free of charge on our website, the full access to all dossiers anytime in the Emprove® library is available through a one-time subscription for 1, 2 or 5 years.

M Lab™ Collaboration Centers

Our M Lab™ Collaboration Centers provide a global network of vibrant collaboration spaces where you can explore ideas, learn innovative techniques and work side by side with experts to solve critical process development challenges. These nine non-GMP labs offer you the flexibility to troubleshoot and test without impacting your production line. Staffed by a network of technical experts, these labs are where we solve your toughest problems — together.

Global Process Development Network

With sites around the world, we can quickly accommodate your evolving needs at a time and a place that works for you. Access the support of our global network of more than 200 scientists, engineers and technicians including process development scientists, biomanufacturing engineers and systems process engineers.

Our Global Network

EXPLORE, LEARN, COLLABORATE

Why Visit an M Lab™ Collaboration Center?

At the M Lab™ Collaboration Centers, no challenge is too great. Our technical expertise spans all aspects of the process train.

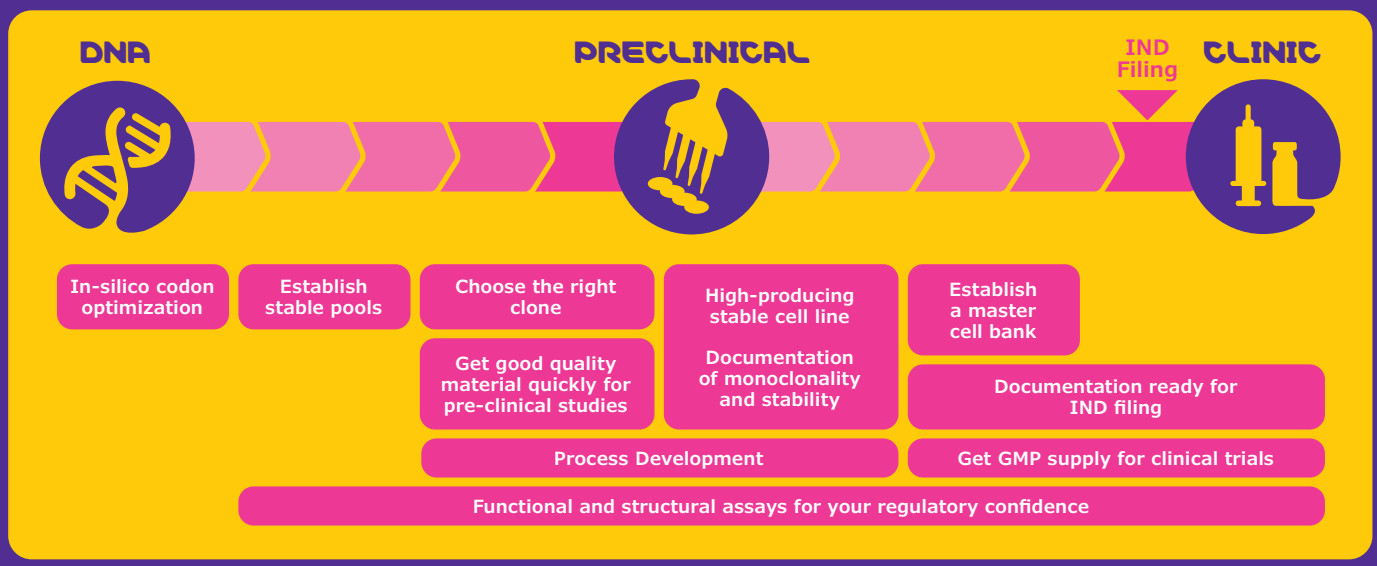
Areas of support we offer include, but are not limited to:

- Overcome barriers to single-use implementation
- Receive guidance for process development and scale up
- Troubleshoot existing processes
- Gain technical knowledge required prior to new product adoption
- Acquire new skills and expertise in bioprocessing and formulation development
- Discover best practices and techniques for adopting next generation bioprocessing
- Develop and test new procedures prior to implementation

TAKE THE RIGHT PATH UPSTREAM

You are developing a monoclonal antibody and a world of potential is ahead of you. However, your time to realize this potential is limited.

You need to act quickly to get your biological drug to market, but have you considered the impact of your decisions as you are developing upstream? Decisions may be difficult to reverse or will require significant backtracking and resources.



Compressed process to get you from DNA to clinic on a reduced timeline.

To successfully advance your molecule from the laboratory to the clinic quickly without sacrificing product quality, process efficiency, or patient safety, you must make the right decisions at the right time; and navigate complexities associated with business planning, cell line development, process development, technology, regulatory and risk assessment.

Our upstream ecosystem—comprised of cell line and media platforms, cell line development, cell line and product characterization services, single-use bioreactors and mixers, process development services, and next generation processing programs—gets upstream development right the first time. Our experts will save you precious time, optimize performance, improve feasibility and sustainability, while laying the groundwork for downstream success.

Learn more at:
MerckMillipore.com/right-path-upstream

You are a biotech startup?
Visit MerckMillipore.com/plug-play-upstream

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