BUILDING A BIOLOGIC
A single cell. Insignificant on its own, perhaps. But when engineered with the correct framework that single cell may be capable of becoming a factory of lifesaving material. With the right support, this individual entity will grow from hundreds to millions to billions of cells, churning out a protein that might one day change the way we prevent, treat or even cure ailments that affect the ones we love.

At Charles River, we see the cell for the valuable building block that it is. As your partner in drug development, we can help you build your biologic through services that support you every step of the way, from cell banking, rapid microbiology and microbial identification solutions through to impurity, potency, biosafety and viral clearance services.

Bringing therapies to the patients who need them is a complex but satisfying journey. Let us be your guide.
CELL BANKING

You have spent years creating a foundation: discovering the correct target, inserting genetic code in just the right place, and modifying cell lines to produce your biologic with precision. Now that you have a solid foundation, you are ready to move forward with creating your master and working cell banks.

Charles River is a partner you can trust to ensure the quality, consistency and integrity of your cell banks. With more than 15 years of experience in GMP cell bank manufacturing, our skilled team is able to provide a smooth and successful outcome for your manufacturing campaign.

- Greater than 1000 cell banks produced for our clients
- Mammalian cell lines, insect cell lines, stem cells
- Aerobic and anaerobic microorganisms

BUILD YOUR BIOLOGIC

Your cell bank is the critical starting point of your production process. By establishing a stable cell bank, you’ll have a standardized cell line free of contamination and genetic drift, providing years of reliable cell performance in your process.

— Austin Lynch
Manager, Manufacturing Services
The characterization of your cell banks is an integral part of ensuring the integrity of your biologic years down the road. Charles River can assist you in determining the most appropriate testing program for characterization studies to provide the information you need to make critical decisions moving forward.

Though many aspects of testing are similar across the industry, our team works to understand your needs. With a mastery of regulatory requirements and a comprehensive portfolio of testing services, we tailor project designs that suit the unique qualities of your cell line.

- Approximately 100 cell banks characterized annually for our clients
- Only AAALAC-accredited facility for in vivo biosafety testing in the United States
- Only GLP TEM provider in the United States

To ensure that you are working with a cell line fulfilling all regulatory requirements, it is important to test your MCB, WCB, EOPC or PPCB according to the international guidelines. For this, Charles River offers the expertise to analyze identity, genetic stability and potential contaminations by viruses, mycoplasma or bacteria.

— Dr. Ilja Quadt
Supervisor, Biosafety & Bioassay Services
The complex infrastructure of biologics leads to specialized methods being needed to determine their potency. *In vivo* and *in vitro* bioassays begin during the early development phase of a biologic with method development efforts and extend throughout its whole life cycle including lot release testing during commercialization efforts.

The intricate nature of large molecules can make it difficult to perform bioassays and achieve reliable results. Charles River delivers consistency with extensive experience in the establishment, validation and conduct of routine bioassays to GMP standards. We provide comprehensive coverage, offering both *in vitro* and *in vivo* bioassays for a variety of biologically active molecules.

- Greater than 750 *in vitro* bioassays performed each year
- Greater than 2100 *in vivo* bioassays performed each year
- Greater than 1000 lot release bioassay tests performed each year

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**BUILD YOUR BIOLOGIC**

*Bioactivity assays should reflect the mechanism of action of a biologic in the patients, and use state of the art technologies to ensure reliable results.*

— Dr. Ulrike Herbrand
Scientific Officer, Bioassays
Safety considerations are part of any well planned construction project. From preclinical lots through routine bulk harvest testing of clinical and marketed batches, contamination testing helps ensure the safety of your biologic before it is released for use in animals and humans.

Charles River offers a portfolio of compendia assays for the detection of mycoplasma and bacterial contaminants and also *in vivo, in vitro* and biochemical viral detection assays. Our experts can design and develop the appropriate testing plan for your biologic, with a selection of available and customized assays that suit your specific needs.

- More than 20,000 reports sent each year from sites across the globe
- Support for more than 200 licensed products
- Fast Track testing for urgently needed results

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**BUILD YOUR BIOLOGIC**

*Testing for adventitious agents, coupled with a thorough risk assessment, is the keystone of biosafety.*

— Dr. James Gombold
Site Director (Malvern, PA)
Residual host cell protein evaluation is a key building block in the preclinical stage of development. Generic assays may be used in preclinical and early clinical stages for impurity detection, but once Phase III studies are reached, a validated assay specific for your product needs to be in place. The findings from this characterization of the purification process are integrated into the CMC section of regulatory filings.

Charles River has the capabilities to support testing of all process stages for impurities such as residual Protein A, DNA, Tween, endotoxin and host cell proteins.

- HCP-GAPex℠ - targeted enhancement of coverage
- In-house polyclonal antisera production from SPF animals
- Multiple offerings for residual DNA assays

Host cell proteins are an inevitable impurity of biopharmaceuticals. Even after multiple sophisticated purification steps, HCPs remain or co-purify with the drug substance. To protect patients from adverse effects, such as immunogenicity, powerful and reliable analytical tools are required to monitor such impurities during the manufacturing process and in final release testing.

— Dr. Olaf Stamm, MDRA
Senior Specialist, Biologics Testing Solutions Europe & Asia
Viral clearance studies are important for reinforcing the structure of your production and purification processes by demonstrating their virus removal potential. Initial studies, concurrent to preclinical studies, must be included in your IND filing, while larger studies begin later in Phase III of your clinical studies for your NDA/BLA filing.

Using a customized approach, we are able to provide technical advice and regulatory support to ensure that a successful and cost-effective program is established and reports are generated to meet your deadlines.

- More than 2100 viral/TSE clearance studies performed
- ICH Q5A, WHO, European, US and Japanese regulatory compliance
- Facilities in the United States and Europe

Dr. Horst Ruppach
Global Manager of Viral Clearance and Global Coordinator of Virology

BUILD YOUR BIOLOGIC

*The efficacy of the first three virus safety barriers for virus entry into a biopharmaceutical product - knowledge, careful material sourcing, and a detailed testing program - cannot compete with the level of virus safety brought into the product with the fourth barrier, a viral clearance program.*

— Dr. Horst Ruppach
Global Manager of Viral Clearance and Global Coordinator of Virology
LOT RELEASE TESTING

Your biologic is built, but as a viable product, its life has just begun. Lot release testing ensures your product’s ongoing safety and efficacy profile, verifying a match with specifications stated in the regulatory paperwork. Moreover, indications that arise in the future may be added to the biologics repertoire, necessitating approval and additions to your license.

Charles River provides release testing services for bulk drug substances and clinical and marketed products and can act as a single site for your global release testing. We are committed to successful long-term relationships with our product release clients and work closely with operational staff, offering flexibility to meet clients’ manufacturing schedules.

- Full specification release testing of more than 500 batches of 20+ final products each year
- Involvement in approximately 20% of all batch releases of biological products sold in Europe
- Product release support for US, EU and other regulatory-distinct markets

BUILD YOUR BIOLOGIC

Manufacturing schedules may not always go as planned. It is important to have flexibility in your lot release testing laboratory to help your supply chain run smoothly and ensure that your biologic gets to the patients that depend on it.

— Dr. Jon Marshall
Site Director (Edinburgh, UK)
The quality of your biologic is assured, but how long will it retain those characteristics? Stability studies play a critical role in all stages of the registration process, starting with your initial IND submission. Later on, stability testing is a key component in the clinical phase of development to be included in your NDA/BLA application, in post-marketing commitments and in support of any future process changes.

Charles River performs stability studies for (bio)pharmaceutical products and drug substances at all stages of the registration process. Over the past 20 years, we have designed and conducted stability testing programs to support early development, formal submission studies per the ICH guidelines, and commitment studies for the continued marketing of existing drug products.

- Included on multiple product licenses approved by the FDA, USDA and EMA authorities
- ICH, sub-ambient and specialized storage conditions available
- Consultation services and troubleshooting expertise

We are all used to ‘best before’ dates on the food we eat, but rarely consider the application of shelf-life in other situations. Biologics have to be routed through a supply chain post manufacture and will be stored in warehouses, pharmacies and potentially in people’s homes. Ensuring products maintain their efficacy throughout this life cycle is the purpose of stability testing.

— Niall Dinwoodie, BSc MSc CChem MRSC QP (IMPs)
Global Coordinator of Analytical Testing
As rewarding as the end result may be, bringing your biologic to market involves a substantial investment of time and money. As you strive to improve efficiencies and reduce costs, it is wise to evaluate strategic sourcing initiatives, including closer collaboration with contractors.

Our RightSource℠ program removes the challenges of externalizing biologics testing by providing customized options that allow you to maintain as much or as little control over your in-house resources, capital assets and facilities that you consider strategic and cost-efficient. We work with you to evaluate your QC testing programs and select the best-suited, most affordable mix of insourcing and outsourcing options.

- Complimentary introductory consultation
- Dedicated, experienced project management staff
- Maintained high visibility of testing activities for clients

Companies struggle with finding a balance between performing work internally and outsourcing it to contract research organizations. It is important to them to keep control of the testing and timelines, but they may not have the technical skills or funding to support it. A mixed insourcing/outsourcing program, such as RightSource℠, allows clients to maintain the visibility they want but offers them an option to introduce cost savings and focus on their core competencies.

— Zane Honnold
Director of Global Sales
The building blocks for specialty biologics such as vaccines and biosimilars share some similarities, but also have many unique attributes compared to other biologics. As an experienced contract laboratory partner, Charles River can guide you along the unique developmental pathways of these products.
Charles River can help you expedite your vaccine development program by providing you with manufacturing support for early-phase clinical trials through lot release programs for commercial products.

SERVICES

- Manufacturing
  - cGMP cell banking
  - virus seed and pilot scale virus preparation
- Cell Substrate/Virus Characterization and Safety Testing
- Potency Assays
- Vaccine Challenge Studies
- Stability Testing
BIOSIMILARS

Charles River delivers client-focused solutions for the specific testing and manufacturing requirements of your biosimilar. Biosimilar production processes are complex, expensive and can be difficult to control, so it is essential to partner with professionals who can perform the full development program while providing the control essential for product uniformity.

MANUFACTURING AND TESTING SERVICES

• Cell Bank Creation and Storage
• Cell Bank and Raw Material Safety Testing
• Potency Testing
• Lot Release Testing
• Stability Testing
• In Vitro Assessment of Immunogenicity: ADA, mAb detection assay, cell-based immunogenicity

SERVICES TO DEMONSTRATE BIOSIMILARITY

• Biophysical Characterization
• Bioassays (in vitro and in vivo): binding assay, ADCC, CDC, apoptosis, other relevant mode of action (MoA) assays
RESOURCES

EMA
EMA/CHMP/BWP/534898/2008: Guideline on the requirements for quality documentation concerning biological investigational medicinal products in clinical trials

EMA/CHMP/BMWP/403543/2010: Guideline on similar biological medicinal products containing monoclonal antibodies – non-clinical and clinical issues

FDA
Characterization and Qualification of Cell Substrates and Other Biological Materials Used in the Production of Viral Vaccines for Infectious Disease Indications (2010)

Points to Consider: Characterization of Cell Lines Used to Produce Biologicals (1993)

WHO

2010 Recommendations for the evaluation of animal cell cultures as substrates for the manufacture of biological medicinal products and for the characterization of cell banks

OTHER
Q5A - Q5E Quality of Biotechnological Products

21 CFR Part 610: General Biological Products Standards

EP 5.2.3 - Cell Substrates for the Production of Vaccines for Human Use (available for purchase through the EDQM Website)
Charles River offers comprehensive testing services to ensure the identity, potency, purity, safety and effectiveness of a biopharmaceutical. We support clients throughout the biologic development cycle, from the establishment and characterization of cell banks through the preclinical and clinical phases.

Take a look into our global biologics testing facilities >>

Learn more about the testing and manufacturing support services that Charles River offers for biologics >>
As a fully integrated partner, Charles River can support your research at any point along the drug discovery continuum.

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LET US HELP BUILD YOUR BIOLOGIC

Your biologic has an impact on the health and wellness of those we love. Because it is important to you, it is important to us. Whether you are in the early stages of your building your biologic or are ready to take it to market, Charles River is an experienced partner, capable of supporting your development every step of the way.