Biologics Testing Solutions

The approval process for ensuring the identity, potency, purity, safety and effectiveness of a biopharmaceutical is complex, but its effective navigation is critical to the ultimate commercial success of your product. With more than 50 years of experience, Charles River Biologics Testing Solutions has the proven knowledge, expertise and capacity to address challenging projects from biotechnology and pharmaceutical companies worldwide. We provide tailored global testing and manufacturing services to help accelerate drug development from concept to product release. Our primary emphasis is on quality, which is enforced through continuous training and internal audit programs, ensuring that our practices are in compliance with global regulatory guidelines. We support clients throughout the biologic development cycle, from the establishment and characterization of cell banks through preclinical and clinical studies to marketed products. We have the capabilities to address the needs of companies based anywhere in the world. Our facilities in the US, UK, Ireland and Germany are part of a global scientific network, offering services that span the entire drug development process. This allows us to provide you with more flexibility, experience and expertise to maximize resources and optimize results based on your specific program needs.

Areas of Expertise Include:

- Cell Banking and Characterization
- Product Characterization
- Impurity Testing
- Viral Clearance Studies
- Lot Release Testing
- Stability Testing
- *In Vivo* Biosafety
- *In Vivo* and *In Vitro* Potency Testing
- Vaccine Challenge Studies
- Polyclonal Antisera Production
- Discovery and Development
- Vaccine Support
- Biosimilar Testing
- Consulting and Project Management

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Cell Banking and Characterization

Cell lines must be tested for the presence of general and specific contaminants to ensure the safety of the associated biological product. Our team of experts works closely with you to develop scientifically sound and cost-effective cell bank programs. We manufacture cell banks for mammalian, microbial, insect, yeast and stem cells and can provide the appropriate cell storage services, all under Good Manufacturing Practice (GMP) guidelines. Our capabilities include purity, sterility, identity, genetic stability testing and an array of other characterization assays from our expansive testing portfolio. Our experienced technical staff can customize your project to create and characterize master cell banks (MCB), working cell banks (WCB), research cell banks (RCB), end-of-production cells (EOPC) and cells at the limit of *in vitro* cell age to fulfill your exact needs and specifications.

Product Characterization

All new biological products need to be characterized prior to inclusion in a clinical trial. The physicochemical characterization of the product includes a range of analytical and molecular methods to elucidate the primary and secondary structure. We have the technical capabilities to support a comprehensive characterization program for inclusion in regulatory filings in the United States, Europe and Japan to support early clinical development programs.

Impurity Testing

The characterization of the purification process is a key part of the chemistry and manufacturing controls (CMC) section of regulatory filings. In support of "quality by design" for any process, testing of residual process impurities is an integral step. We have the capabilities to support testing of all process stages for impurities such as residual Protein A, DNA, Tween, endotoxin and host cell proteins. Generic methods are offered, as well as transfer or method development and validation for customized, product-specific methods.

Viral Clearance Studies

All manufacturers of biologics are required to assess the ability of the manufacturing process to generate a product safe for human use. Therefore, a viral clearance study is performed to evaluate key steps of the manufacturing process to ensure that it is effective at removing or inactivating viruses. Our scientists, located in both Europe and the United States, have extensive experience in the design and performance of viral clearance studies, including TSE clearance, for a wide range of products. We take a customized approach that includes advice and regulatory support in the selection of process steps and model viruses, scaling-down of purification processes and subsequent design of study protocols to ensure a successful program is established and reported to meet your timelines.

Lot Release Testing

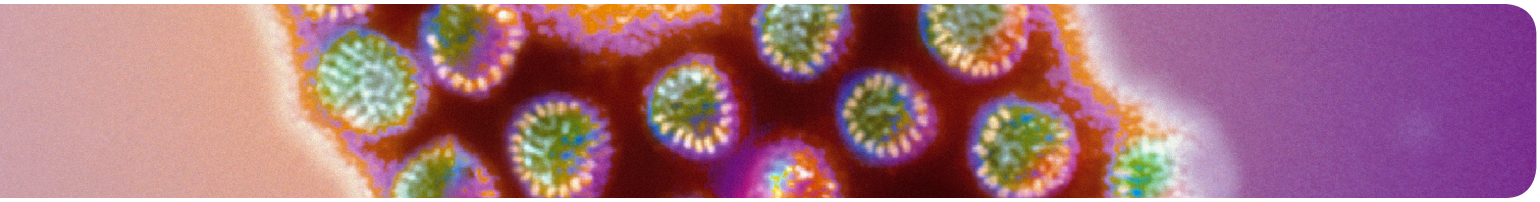
All products entering domestic or global pharmaceutical markets require GMP testing to ensure that they are released in accordance with approved specifications. Release testing packages are composed of a range of studies previously validated to demonstrate compliance of the product. Charles River provides release testing services for bulk drug substances and clinical and marketed products for the European Union (EU), United States (US) and other regulatory-distinct markets, and can act as a single site for your global release testing. We provide a full range of support, including analysis using suitable *in vivo* and *in vitro* potency assays, microbiology tests, and pyrogen and monocyte activation testing (MAT) to determine purity, identity and other biochemical characteristics.

Stability Testing

Biological products have distinguishing characteristics, and the quality of these products must be tested under a variety of environmental factors, such as temperature, humidity and light, in order to confirm their stability during the intended storage period. We provide drug substance and final product *in vivo* and *in vitro* stability testing and storage services in compliance with current International Conference on Harmonisation (ICH) guidelines to support clinical studies, license applications and post-marketing commitments.

In Vivo Biosafety

To help with safety evaluation, we provide *in vivo* testing in our AAALAC-accredited *in vivo* biosafety (IVB) testing services laboratories according to GMP guidelines. IVB testing services include mouse/rat/hamster antibody production (MAP/RAP/HAP), inapparent virus assays, tumorigenicity testing and general safety testing.



In Vivo and *In Vitro* Potency Testing

Potency determination is necessary for regulatory submission and lot release of all biopharmaceutical products. We can aid in the development of an *in vivo* potency assay through range-finding studies using investigation parameters, such as dose level and route of administration, followed by validation and implementation. We also have experience conducting *in vivo* bioassays to show efficacy and safety. These assays include adjuvant assessment, lot release potency testing, bacterial and vaccine challenge studies, and stability testing for a diverse range of products, including hormones, vaccines, neurotoxins, allergens, antivenom, bacteria and blood products.

In vitro bioassays can also be used to determine the potency of a biopharmaceutical by comparing the biological response related to its mode of action with that of a control preparation. We offer cell-based bioassays for the determination of potency of EPO, PTH, G-CSF, GMCSF, interferon and multiple monoclonal antibodies. With extensive experience developing bioassays for monoclonal antibodies, Charles River is also able to provide expert opinions and support for the analysis of biosimilars. Assays for many biosimilars have already been developed and optimized by our team of scientists and, after discussions, can be adapted to your particular compound.

Vaccines Challenge Studies

Experience with *in vivo* bacterial and vaccine challenge studies has become an important element of the Discovery and Development Department. Designing an animal challenge study that will translate to humans requires consideration of route of infection, infectious dose, permissive animal species, vaccine formulation, biomarkers, immune responses and disease endpoints. Charles River is currently conducting *in vivo* challenge studies with certain BSL-2 pathogens. To ensure our commitment to humane care, there are important regulations, animal ethics and safety considerations we address when working with pathogens. We have recently completed a new high biosecurity containment facility for the conduct of bacterial challenge studies. Charles River scientists from our Microbiology, Discovery and Development, Biologics and Preclinical (toxicology and pathology) Services groups assist sponsors in these nonclinical and regulatory aspects of vaccine development.

Polyclonal Antisera Production

Charles River offers polyclonal antisera production in a variety of species, such as rodents and farm animals (sheep and goats are the most commonly used). Projects can be customized to client-specific requirements and current cGMP standards. Other product types available include defibrinated blood products, whole blood in anticoagulant (sodium citrate, Alsever's, heparin), serum, plasma and lysed blood.

Discovery and Development

Custom method development and technology transfer are key strengths of Charles River. We assist both large clients and clients with limited in-house resources in evaluating candidate products. Information obtained is used by clients to assess their products and determine which to take forward to larger studies. Our groups can also support you in meeting novel or changing requirements with assay design, development, optimization and validation, as well as routine testing. The assays are customized to your needs and include molecular, cell-based or protein-based assays. Technical transfer of assays can also be performed at our sites.

Vaccines

As part of the Charles River vaccine program, we utilize expertise from our global scientific network to provide vaccine companies with considerable flexibility and convenience in the development of their products. We have experience in the manufacture of live and attenuated viral vaccines and challenge viruses in cell-based expression systems under Good Manufacturing Practice (GMP) requirements for both preclinical studies and early-phase clinical trials. We offer testing from release of cell banks and viral stocks to the release of bulk and final vaccine product.

Biosimilar Testing

Our experience working with biologics across the drug development continuum, together with our scientific and regulatory expertise, makes Charles River an ideal partner for your biosimilar development. We deliver client-focused solutions for the specific testing and manufacturing requirements of your biosimilars. Services include cell bank creation and storage, cell bank characterization, safety testing, process evaluation for viral clearance, product characterization, stability studies, equivalence studies and product release testing. We also offer bioassays and mass spectrometry services to demonstrate comparability.

Our Preclinical Services Group offers a full range of services needed for biosimilar development, including toxicology studies to demonstrate biosimilarity, analytical (dose formulation analysis) and bioanalytical assays (toxicokinetics and immunogenicity), immunohistochemistry (e.g., tissue-cross reactivity) and immunology (e.g., flow cytometry and other biomarkers as appropriate).

Consulting and Project Management

As part of the Charles River services portfolio, our consulting group provides regulatory as well as CMC consulting to help you plan, anticipate and navigate the challenges of bringing a biological product to market. Our integrated approach can provide reductions in both time and cost by generating the most appropriate information for rapid decision making. We understand that delivering a biologic to the market can be a challenging and time-sensitive process. Charles River believes in constant and relevant communication to ensure that clients are informed every step of the way. We are committed to providing the best possible service and individual care, including dedicated project managers, to accelerate the development of your biologic from discovery testing through to product release.

Partnerships

At Charles River, our goal is to provide clients with a wide range of services that meet their regulatory and scientific needs. The following partnerships with industry leaders in specialty areas enhance our capabilities by offering seamless, cost-effective and innovative solutions that accelerate the production and safety assessment of biopharmaceutical products.

MILLIPORE

EMD Millipore, the life science division of Merck KGaA of Darmstadt, Germany, partners with Charles River to exclusively license EMD Millipore's TrueSpike™ technology. EMD Millipore and Charles River collaborate to integrate the TrueSpike™ technology into client-specified viral clearance projects provided by Charles River. This collaboration is designed to result in a more predictable and consistent study outcome for clients and to ultimately help improve drug product safety.

PROTAGEN

Our partnership with Protagen AG, a GMP-certified specialist in the characterization of protein drugs, provides clients with services covering the entire range of protein analytics, from detailed protein characterization to stability and lot release testing. Protagen's experience with biosimilar comparability testing complements Charles River's existing testing portfolio to move your biosimilar development forward. Working together, Charles River and Protagen offer analytical experience and superior services through a single point of contact, providing more efficient project work and study design.

GENEWIZ

GENEWIZ, Inc. works with Charles River to provide a single point of contact offering next-generation sequencing to complement the manufacturing and characterization of a client's cell and virus bank. Clients benefit from this partnership by receiving Charles River's expertise and experience in cell and viral bank characterization with the added option of GENEWIZ's industry-leading next-generation sequencing service.

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