

Biopharmaceutical Services

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 Biopharmaceutical Services (BPS) 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.

BPS has the capabilities to address the needs of companies based anywhere in the world. Our BPS facilities in the US, UK, Ireland, and Germany are part of a global scientific network, offering products and 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
- Process Characterization (Residual Testing)
- Vaccines and Cell Therapy
- Viral Clearance and TSE Studies
- Lot Release Testing
- Stability Testing
- *In Vivo* Biosafety
- *In Vivo* and *In Vitro* Potency Testing
- Biosimilar Testing
- Discovery and Development
- Polyclonal Antisera Production
- Consulting and Project Management



Cell Banking and Characterization

Cell lines must be tested for the presence of general and specific contaminants to ensure the safety of the resulting 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 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 physiochemical 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 US, EU and Japan to support early clinical development programs.

Process Characterization

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

Vaccines and Cell Therapy

As part of the Charles River vaccine program, we utilize the expertise from our global scientific network to provide vaccine companies with considerable flexibility and convenience in the development of their products. We have many years of experience working with various cell substrates and viruses, as well as the preparation of vaccines for clinical trials, utilizing egg and cell-based production methods. Our capacity enables up to 5,000 vials per batch with either manual or semi-automated filling. To meet future demands, we have a state-of-the-art, 10,000-square-foot GMP manufacturing facility. We are constantly adopting new technologies in this facility and have disposable cell culture systems to meet your needs.

Viral Clearance and TSE 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 each step of the manufacturing process to ensure that it is effective at removing or inactivating viruses.

Our scientists, located in both Europe and the US, have extensive experience in the design and performance of viral clearance studies, including TSE, for a wide range of different 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 the 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. BPS provides product release for the European Union, US, and other distinct regulatory markets. We provide a full range of support, including analysis using suitable *in vivo* and *in vitro* potency assays, microbiology tests, 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 to confirm their stability during the intended storage period. BPS provides 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 accredited *in vivo* biosafety (IVB) testing services laboratories according to Good Laboratory Practice (GLP) and GMP guidelines. IVB testing services include Mouse/Rat/Hamster Antibody Production (MAP/RAP/HAP), Inapparent Virus Assay, Tumorigenicity Test and General Safety Test.

In Vivo and In Vitro Potency Testing

Potency determination is necessary for regulatory submission and lot release of all biopharmaceutical products. BPS 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, bacterial and viral challenge studies, and stability testing for a diverse range of products, including hormone potency assays, vaccines, neurotoxins, allergens, anti-venom, 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, GM-CSF, interferon and monoclonal antibodies.

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), bioanalytical (toxicokinetics and immunogenicity), immunohistochemistry (e.g., tissue-cross reactivity), and immunology (e.g., flow cytometry and other biomarkers as appropriate).

Discovery & Development

We evaluate candidate products for large clients as well as clients with limited capacity or resources in-house. Information obtained is used by clients to assess their products and determine which ones to take forward to larger studies. Other activities within the department include adjuvant assessment, assay design development and validation, efficacy testing and assessment of different routes of administration. We adhere to R&D, GMP and GLP guidelines.

Custom method development and technology transfer are key strengths of the Discovery & Development department. Charles River has over 15 years of experience in method development. Our groups can 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, virological or protein-based assays. Technical transfer of assays can also be performed at our sites.

Experience with *in vivo* bacterial and viral challenge studies has become an important element of the Discovery & 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. Since pathogens are involved, there are important regulations, animal ethics and safety considerations to address to ensure the ultimate in humane care for the animals—a global priority at our labs. 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, Biopharmaceutical and Preclinical (toxicology and pathology) Services groups assist sponsors in these nonclinical and regulatory aspects of vaccine development.

Polyclonal Antisera Production

Charles River BPS 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.

Consulting and Project Management

As part of the Charles River services portfolio, our Navigators consulting group provides regulatory as well as CMC consulting to help you plan, anticipate, and

navigate through the challenges of bringing a biological product to market. Our integrated approach can provide reductions in both time and cost by generating more appropriate information for rapid decision-making.

We understand that delivering a biologic to the market can be a challenging and time-sensitive process. BPS 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. Charles River is your ideal collaborative partner.

