charles river

BIOLOGICS TESTING SOLUTIONS

Comprehensive Services for Biologics Developers and Manufacturers

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 product's ultimate commercial success. With more than 50 years of experience, the Charles River Biologics Testing team 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 continual training and internal audit programs to ensure that our practices are in compliance with global regulatory guidelines. We support clients throughout the biologic development cycle, from discovery through preclinical and clinical studies to marketed product release. We have the capabilities to address the needs of clients based anywhere in the world and have specialized programs for companies that focus on vaccine, cell therapy and biosimilar development. Our facilities in the United States, United Kingdom, Ireland, France and Germany form a global scientific network, allowing us to provide our clients with flexible, comprehensive solutions to maximize resources and optimize results.

Areas of expertise:

- Cell banking and characterization
- Product characterization
- Impurity/Residual testing
- Viral clearance studies
- Lot release testing
- Stability testing
- *In vivo* biosafety
- *In vivo* and *in vitro* potency testing
- Vaccine challenge studies
- Monoclonal/Polyclonal antisera production
- Biosimilar testing
- Vaccines
- RightSource[SM]
- Consulting and project management

EVERY STEP OF THE WAY

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 collaborates with clients 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 a project to create and characterize master cell banks, working cell banks, research cell banks, end-of-production cells and cells at the limit of *in vitro* cell age, according to client 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 support the development of complex biologics and biopharmaceuticals through expertise in structural and functional characterization programs for inclusion in regulatory filings in the United States, Europe and Japan.

Impurity/Residual 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 support testing of all process stages for impurities such as residual Protein A, DNA, Tween, IPTG, TRIS, PEI, endotoxin and host cell proteins. In addition to generic methods, we offer 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 have extensive experience in the design and performance of viral clearance studies, including transmissible spongiform encephalopathy (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 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 include a range of studies previously validated to demonstrate compliance of the product. Charles River provides release testing services for bulk drug substances, as well as clinical and marketed products for the EU, US and other regulatory-distinct markets, and can unify global release testing with a single provider. We provide a full range of support, including analysis using suitable *in vivo* and *in vitro* potency assays, analytical and microbiology tests, and pyrogen and monocyte activation testing (MAT) to determine purity, identity and other biochemical and biophysical characteristics.

Stability Testing

Biological products have distinguishing characteristics, and the quality of these products must be tested under a variety of environmental factors (e.g., temperature, humidity, light) in order to confirm their stability during the intended storage period. We provide drug substance and final product 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* biosafety (IVB) testing in our AAALAC-accredited laboratories according to GMP guidelines. IVB testing services include mouse/rat/hamster antibody production (MAP/RAP/HAP), inapparent virus assays, tumorigenicity testing and abnormal toxicity/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 (e.g., dose level and route of administration), followed by validation and implementation. We also conduct *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 many types of products, including EPO, PTH, G-CSF, GM-CSF, interferon and multiple monoclonal antibodies. With extensive experience developing bioassays for monoclonal antibodies, we can readily support the analysis of biosimilars and adapt or optimize existing assays to suit the needs of a particular product.

Vaccine Challenge Studies

Experience with *in vivo* bacterial and vaccine challenge studies has become an important element of drug discovery and development. 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 conducts *in vivo* challenge studies with BSL-2 pathogens. Observing our commitment to humane care, we address all regulations, animal ethics and safety considerations when working with pathogens. Scientists from our Microbiology, Discovery, Biologics and Safety Assessment groups assist sponsors in these nonclinical and regulatory aspects of vaccine development.

Monoclonal and Polyclonal Antisera Production

Charles River offers monoclonal and 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 meet client requirements and GMP standards. Other product types available include defibrinated blood products, whole blood in anticoagulant (sodium citrate, Alsever's, heparin), serum, plasma and lysed blood.

Biosimilar Testing

With decades of success in building biologics, Charles River is likewise an ideal partner in the development of biosimilars. We deliver client-focused solutions for the specific testing and manufacturing requirements of biosimilars. Services include cell bank creation, characterization and storage, biosafety testing, process evaluation for viral clearance, originator and biosimilar product characterization, including mass spectrometry, originator and biosimilar unstressed and forced degradation comparability studies, stability studies, equivalence studies, bioassays and product release testing. In addition, as a contract research organization with true end-to-end capabilities, our Safety Assessment team can enhance efficiencies by providing the necessary services with a range of tests to support the development process. These can include 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).

Vaccines

As part of the Charles River vaccine program, we draw from our global scientific network to provide vaccine companies with considerable flexibility and convenience in the development of their products. We manufacture both live and attenuated viral vaccines and challenge viruses in cell-based expression systems under 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 products.

RightSource℠

Combining 20 years of experience in facility management, staffing and consulting services with a long-standing history of operating quality control testing laboratories makes Charles River the best choice for our clients' scientific staffing needs. The Charles River RightSource℠ scientific staffing program is a flexible insourcing/outsourcing option for biologics developers and manufacturers. The RightSource℠ program removes the challenges of externalizing biologics testing by providing customized options that allow clients to maintain as much or as little control over their in-house resources, capital assets and facilities that they consider strategic and cost efficient. We work with clients to evaluate quality control testing programs by reviewing their current testing structure and selecting the best-suited and most cost-efficient mix of insourcing and outsourcing options.

Consulting and Project Management

As part of the Charles River services portfolio, our consulting group provides regulatory as well as CMC consulting to help clients plan, anticipate and navigate the challenges of bringing a biological product to market. Our integrated approach can both save time and reduce costs by generating the most appropriate information for rapid decision making. Our dedicated project managers believe 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 to accelerate biologics development from discovery testing through to product release.

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askcharlesriver@criver.com • www.criver.com