

## Pathology Services

A comprehensive assessment of pathologic changes is integral to preclinical and clinical studies for determining safety, efficacy, and mechanism of action of novel therapeutic agents. Pathology end points are critical for maintaining experimental animal colonies and characterizing disease models utilized in the drug discovery and development process.

Charles River Pathology Associates features the largest collective assembly of contract pathologists in the industry. Our state-of-the-art technology and multidisciplinary expertise with nearly all types of drugs, biologics, and devices enable us to offer a wide array of routine and specialized pathology services either in support of in vivo studies performed within Charles River or as a stand-alone service with samples received directly from our clients. Our pathologists are recognized experts in toxicologic pathology, carcinogenesis research and testing, and diagnostic pathology in support of IND-enabling research and safety programs.

- Toxicologic Pathology
- Peer Review
- Clinical Pathology
- Archive/Repository
- Bone and Joint Pathology
- Medical Device Pathology
- Electron Microscopy
- Immunohistochemistry
- Histomorphometry
- Tissue Cross-Reactivity
- Neuropathology
- Molecular Pathology

In addition to our unique pathology support, Charles River provides the most flexible product-specific resources in the preclinical testing arena. These complementary integrated resources range from consulting, program design, and regulatory guidance to research, efficacy, and safety programs.

Standardization of pathology procedures and stringent quality control measures ensure consistency and accuracy. Our activities and evaluations are conducted in compliance with international regulatory standards and designed to meet the evolving requirements for developing products worldwide.



## Toxicologic Pathology

Charles River operates full-service laboratories with facilities and program/project offices at numerous locations around the globe. All of the facilities are functionally integrated and offer interactive services to fulfill your needs. Each of the laboratories is equipped to provide complete GLP-compliant necropsy, histology, and histopathology, and many offer a wide variety of specialty pathology-based services to support your research programs.

- Necropsy
- Histology
- Histopathology
- Peer review

## Peer Review

Our senior veterinary pathologists have been actively participating in formal quality assessment and peer review programs since 1982. Today, Charles River pathologists are recognized experts in toxicologic pathology, carcinogenesis research and testing, and diagnostic pathology in support of IND-enabling research and safety programs. To date, we have conducted more than 750 peer review and quality assessment efforts on more than 500 chemicals, drugs, and biomedical devices for government and commercial clients.

## Clinical Pathology

At Charles River, a complete range of clinical pathology laboratory services is available to support preclinical studies and clinical trials. Toxicology studies are supported by an extensive array of safety assays and investigative biomarkers. These assays have been established to aid in the early identification of toxicity and efficacy of test articles and, where appropriate, can be transferred into the clinical phase of development for human use.

- Clinical chemistry
- Hematology
- Hormone assays
- Coagulation/hemostasis/platelet aggregation
- Urinalysis
- Microbiology
- Immunoassays
- Blood gas analysis

## Archive/Repository

The commercial archive and repository units at Charles River have been providing GLP-compliant data and sample archiving services in support of preclinical and clinical studies for decades. We offer strategically located facilities and services to provide short- and long-term (30-year) materials storage for government and private sector businesses, organizations, and consortia.

- Short- and long-term storage
- Inventory, tracking, and expedient retrieval utilizing a custom-designed computerized system
- Specimen and materials preparation and storage
- Preparation for storage and retention by our staff at either your or our facility
- Material transport
- Scheduled documented inspections of materials
- Hard-copy data transfer to CD-ROM

## Bone and Joint Pathology

Charles River provides comprehensive bone, cartilage, and hard tissue pathology-based services to support the evaluation of metabolic bone diseases, arthritis, and orthopedic devices. Our experienced pathologists and scientists, together with a team of highly trained technicians, provide study design and project execution services for therapeutics devised for the treatment and prevention of osteoporosis, arthritis, and bone and cartilage healing.

- Decalcified paraffin processing
- Undecalcified bone embedding
- Bone labeling technique
- Organ and tissue morphology
- Cellular and molecular changes
- Histomorphometry
- Radiography
- Bone densitometry
- Biomechanical strength testing

## Medical Device Pathology

Charles River supports developers and manufacturers of medical devices from the proof-of-concept stage to pivotal safety and efficacy evaluations. We offer an integrated approach to medical device studies with a commitment to scientific excellence, an appreciation for client-specific issues, and an understanding of regulatory considerations.

Our technicians and pathologists can prepare and evaluate all categories of devices: external devices (intact as well as breached or compromised surfaces), external communicating devices (intact natural channels, plus indirect and direct blood paths), and internal devices (bone, tissue and fluid, and blood). Enhanced by our expertise in anatomical and clinical pathology and our state-of-the-art laboratories, Charles River has become the leader in providing support to device manufacturers.

- Protocol preparation and review
- Necropsy support
- Sample preparation
- Plastic embedding
- Sectioning of hard materials
- Histopathology
- Photographic documentation
- Morphometric evaluation
- Imaging

## Electron Microscopy

Charles River offers full-service electron microscopy with both transmission and scanning capabilities in multiple locations. These instruments use a focused beam of electrons instead of light to examine a specimen at a very detailed level to gain information as to its structure and composition.

- Transmission electron microscopy (TEM)
- Scanning electron microscopy (SEM)
- Light microscopy
- Dual-energy X-ray absorptiometry (DEXA)
- Quantitative computed tomography (QCT)
- Micro-computed tomography (Micro-CT)
- Digital radiography

## Immunohistochemistry

Charles River is the acknowledged leading contract research organization within the biopharmaceutical community for providing state-of-the-art specialized pathology and related technologies designed to address the specific efficacy and safety needs of novel therapeutic classes. Pathology-based technologies are used to address mechanistic, cell response characterization, and issue-driven needs of a comprehensive array of therapeutic modalities and chemical classes. We recognize immunohistochemistry as a valuable tool used to localize cellular expression of specific proteins within the context of the tissue.

- Tissue cross-reactivity testing of monoclonal antibody therapeutics
- Angiogenesis
- Cell proliferation and apoptosis
- Biomarkers
- Xenotransplantation therapies
- Immunophenotyping

## Histomorphometry

Histomorphometry is a highly specialized technique of stereology that utilizes the latest technology in microscopy and image analysis software to describe and evaluate changes in tissue morphology. This technique is applied to tissues and biomaterials of all types to measure tissue or device area, perimeter, linear and curvilinear distances; to describe cellular proliferation; and to quantify image density for molecular and cellular pathology. Charles River recognizes the need for special techniques such as histomorphometry to further evaluate and quantify histopathologic changes in tissues in support of government and commercial pathology service efforts and for molecular and cellular pathology.

## Tissue Cross-Reactivity

Charles River can support your monoclonal antibody research with our extensive expertise in the initial stages of safety assessment for therapeutic antibodies targeted for use in humans. We have experience with nearly every type of therapeutic antibody, including unconjugated antibodies, antibodies conjugated to a variety of substances, and Fab fragments.

- Preliminary studies
- Definitive study
- Extensive controls
- Slide evaluation and interpretation
- Internal peer review
- *In vitro* cross-reactivity
- *In vivo* binding of test articles
- Analysis of potential treatment-related effects
- Immunophenotyping

## Neuropathology

Charles River combines world-class neuropathologists with highly trained technical staff to offer specialized services in neuropathology. We provide assistance in study design, development strategies, and regulatory submissions for a wide variety of compounds, viruses, genes, and stem cell introductions affecting the nervous system.

- Whole-body perfusion
- Large brain sectioning
- Nerve tissue embedding
- Subanatomic detail
- Specialized staining
- Immunohistochemistry
- Imaging
- Ultrastructural analysis
- Electron microscopy (EM)
- Magnetic resonance microscopy (MRM)
- Morphometric analysis

## Molecular Pathology

By combining a strong history in molecular biology and histopathology, Charles River can relate gene expression to tissue histomorphology in both normal tissues and therapeutic models of disease, providing you with valuable functional genomics information. The end result is the best possible interpretation and troubleshooting of molecular-based tools, such as in situ hybridization and real-time quantitative polymerase chain reaction (Q-PCR), applied to toxicological pathology issues.

- *In situ* hybridization
- *In situ* gene expression studies
- PCR
- Real-time Q-PCR studies

In addition to our pathology support, Charles River offers expert consulting and in-life services to help guide your therapeutic through a seamless transition to the preclinical and clinical stages. With our extensive experience covering a wide range of compounds and our global regulatory expertise, we can offer innovative solutions and strategic program advice to efficiently and effectively accelerate your research and drug development, exactly.