

PATHOLOGY SERVICES

Comprehensive assessment of pathologic changes is critical for the evaluation of toxicology and research studies, as well as for animal colony maintenance. With more than 40 toxicologic pathologists, Charles River Laboratories Discovery and Development Services is able to offer the most extensive resources and expertise dedicated to pathology-based support of our clients' product discovery and development activities. Our multidisciplinary expertise, state-of-the-art technology, and depth of experience with large and small molecules and devices enable us to offer a wide array of integrated services ranging from consulting and program design to research, efficacy, and safety programs through regulatory guidance. By offering these and other specialty pathology services, Charles River provides the most flexible, timely, and cost-effective product-specific resources available in the industry. All evaluations are conducted in compliance with Good Laboratory Practices (GLP) unless otherwise indicated.

Toxicologic Pathology

- Over 40 dedicated veterinary pathologists
- Experimental and toxicological pathology
- Discovery/lead optimization pathology
- Diagnostic pathology

Preclinical Product Development Consulting

- IND-enabling and NDA-supporting program design
- Product-specific regulatory guidance

GLP Archive/Repository

- Security-controlled storage of biological specimens and data
- Low-temperature storage

Monoclonal Antibody Characterization

- Early stage safety assessment for humanized monoclonal antibodies targeted for human therapy
- IND-required cross-reactivity protocols

Bone and Medical Device Pathology

- All aspects of device response are evaluated
 - Hard and soft tissue plastics histology
 - Organ, tissue, cellular, and molecular changes
 - Digital quantitative image analysis

Developmental and Reproductive Toxicology (DART)

- Assessment of male and female reproductive toxicology
- Assessment of *in vivo* and *in vitro* developmental toxicology
- Mobile services offering specialists, all instrumentation, and validated technologies to conduct critical endpoint measurements at client sites

Peer Review Pathology

- Nearly 700 peer review/quality assessment efforts conducted on more than 500 chemicals, drugs, and biomedical devices in virtually all species and routes of delivery

Regulatory-Required ToxPath Services

Histologic evaluation of tissues from multiple species

- 40 plus board-certified veterinary pathologists
- Specialists in all major organ systems, disease states, and therapeutic agents

Routine and special staining techniques

- Standard H&E histology
- GMA and MMA plastics histology
- Enzyme histochemistry
- Immunohistochemistry
- *In situ* hybridization
- Molecular pathology

Routine and special necropsy procedures

- All applicable species
- All aspects of necropsy procedures
 - Special tissue harvest
 - Whole body or organ perfusion technology





Specialty Pathology Services

Transgenic Phenotyping Pathology

- Characterize gross and microscopic morphology, cell proliferation and apoptosis, as well as gene expression in embryos and fetuses from genetically-altered mice

Clinical Trials Support Services

- Correlative lab studies identify surrogate biomarkers of efficacy, confirm mechanism of drug action, and validate animal models.

Cell Kinetics (apoptosis, cell proliferation)

- Cell kinetic assays quantify the relative rates of cell death and/or cell division within a target tissue.

Immunohistochemistry

- Tissue sections stained with antibody markers detect cell proliferation, apoptosis, angiogenesis, expression of specific gene products, or cellular identification.
- Tissue localization of proteins, enzymes, nucleic acids, and other subcellular structures

In situ Hybridization

- Tissue sections stained with chemically- or radioactively-labeled nucleic acid probes detect vector delivery and localization, transgene expression, and alterations in endogenous gene expression.
- Quantitative PCR

Flow Cytometry

- Lymphocyte subsets in blood and lymphoid tissues

Neuropathology

- All applicable species
- *In situ* intravascular perfusion, dissection, and handling of nervous system tissues
- Special dissection techniques for location and removal of tissues from the central, peripheral, and autonomic nervous systems

Histomorphometry/Image Analysis

- Stereology utilizing the latest technology in microscopy and image analysis software to describe and quantitatively evaluate changes in tissue morphology

Ultrastructural Pathology (SEM/TEM)

- GLP-consistent transmission and scanning electron microscopy (TEM and SEM, respectively) services for viral particle tabulation, quantitation, and characterization in support of IND and NDA applications

Whole Embryo Culture (WEC) Screening Assay

- *In vitro* developmental toxicity testing using an established WEC technique

Clinical Pathology

- Evaluation of laboratory animal blood samples for hematological and clinical chemistry parameters
- Urine for urinalysis
- Tissues and body fluids for a wide variety of specialized enzyme determinations
- Blood gas analysis
- CO-oximetry
- Coagulation
- Cytology



CHARLES RIVER
LABORATORIES

Discovery and Development Services

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