charles river

FACILITY OVERVIEW

Pathology Associates, North America

Our Pathology Associates division hosts a collective group of scientists dedicated to pathology support for the investigation of any type of biopharmaceutical, chemical or medical device. Experienced pathologists located at multiple sites can analyze pathology from any investigative or safety assessment study.

Background

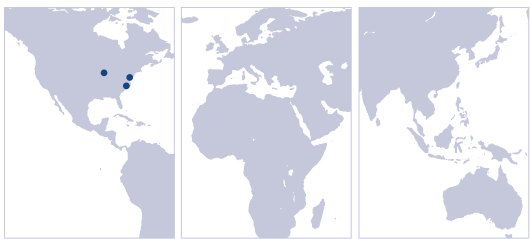
- Founded in 1981
- Acquired by Charles River in 2001
- Comprises three separate laboratories located in Maryland, Illinois and North Carolina

Laboratories and Facilities

- 52,000 square feet/15,850 square meters of total combined laboratory space
- 10,000 square feet/3,050 square meters of central archives
- Recent investments into laboratory infrastructure and material space
- Four dedicated transmission electron microscopy (TEM) rooms
- Laboratories
  - Toxicologic pathology
  - Immunopathology
  - Electron microscopy
  - Medical device
  - Reproductive toxicologic pathology
  - Image analysis/morphometry/stereology

Service Areas/Study Types

- GLP and non-GLP study conduct
- Toxicologic pathology
  - Experimental animal models, organ systems, routes of exposure, testing designs, therapeutic agents and diseases
  - Routine histology
  - Special stains
  - Juvenile histology and pathology
  - Neurohistology and neuropathology
  - Radiation pathology
- Necropsy support
  - Traveling necropsy team in North America
  - Specialized tissue collection
- Monoclonal antibody cross-reactivity testing (GLP-compliant human tissue cross-reactivity testing)
- Tissue-based biomarkers
  - Immunohistochemical detection of protein markers in tissues
  - Markers for angiogenesis, growth factors and receptors, cell proliferation and apoptosis
  - Test article biodistribution
  - GLP-compliant immunohistochemistry conducted for the detection of the test article as well as possible nonhuman primate antihuman immune and/or inflammatory responses
  - Methods developed to allow similar evaluations on rodent and rabbit tissues



EVERY STEP OF THE WAY

Service Areas/Study Types (Continued)

- Medical device pathology
  - GLP-compliant necropsy, sample preparation and histopathology evaluation with digital imaging
  - Plastic embedding and sectioning of all types of biomaterials, including intact stents and bone devices/materials
- Electron microscopy
  - GLP-compliant services
  - Ultrastructural morphology procedures allow visualization of unique structure details and quantification of cellular organelles and subcellular structures
- Reproductive toxicologic pathology services
  - Customizable GLP-compliant multispecies mobile sperm analysis capabilities
  - Male reproductive pathology
  - Female ovarian follicle quantification
- Image analysis/morphometry
  - Whole slide scanning with online slide viewing capabilities
  - Whole-slide morphometric analysis directly on scanned slides using GLP-validated Visiopharm software
  - Linear and area measurements, image analysis on immunohistochemically or histochemically stained slides, cell proliferation and apoptotic index determination, morphometry for developmental neurotoxicity studies
- Stereology
  - Full-range of services for discovery and GLP-compliant studies
  - Systematic uniform random sampling and analysis of tissues of any size from all species
  - Experience with paraffin-embedded, plastic-embedded, or frozen tissues
  - Object counting using physical or optical disectors; estimation of volume for tissues, tissue compartments or cells; and estimation of surface area and length
- *In situ* hybridization
  - Detection of mRNA
  - Use of RNAscope® technology on GLP-validated automated staining instruments
- Tissue microarrays
  - Creation of array blocks and slides
  - Customizable to client needs, including tissue types, number of pieces of each tissue, etc.
  - Staining of array slides with immunohistochemistry or *in situ* hybridization for detection of protein or mRNA, respectively
- GLP-compliant immunohistochemistry services
  - QIHC certified technical staff
  - Assay development for novel and unique antibodies
  - State-of-the-art automated staining instruments
  - Double staining
- GLP-compliant archive/repository
  - Controlled access, redundant security systems and continuously monitored environmental control system
  - Emergency power systems provide backup for security, fire detection/suppression, HVAC systems and storage freezers
  - Inventory and retrieval computer system

Compliance, Certifications, Accreditations and Professional Affiliations

Charles River's Pathology Associates' sites operate in compliance with the requirements of the following regulatory agencies or accredited organizations:

- U.S. Environmental Protection Agency (EPA)
- U.S. Food and Drug Administration (FDA)
- European Medicines Agency (EMA)
- Japanese Pharmaceuticals and Medical Device Agency (PMDA)

Quality and Process Initiatives

- Lean Six Sigma programs
- On-site IT support and backup
- Validated electronic data collection (Provantis™)
- Ability to enter findings into client data collection system
- Forefront of FDA Standard for the Exchange of Nonclinical Data (SEND) initiative
- Electronic audit routing and approval quality management system
- Excellent regulatory compliance history

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