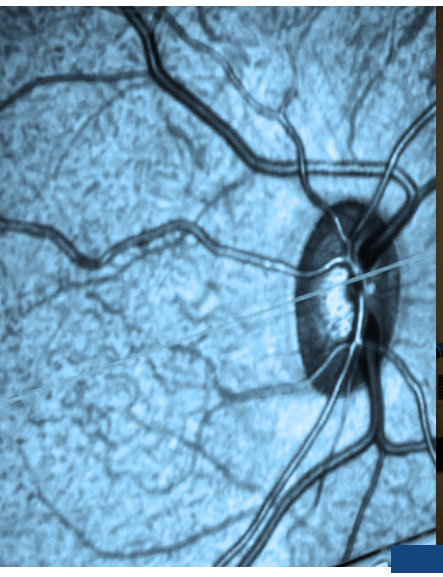
charles river



Supporting the Discovery & Development of Ocular Drug Products

Pharmacology/Efficacy Models

In Vivo Models:

- Age-related macular degeneration
- General anti-VEGF model
- Glaucoma (normotensive/ hypertensive) models
- Neuroprotection
- Uveitis
- Automimmune uveitis
- Sjogrens syndrome

In Vitro Models:

- Ocular irritation and severe damage
  - MatTek EpiOcular™
  - Bovine corneal opacity & permeability (BCOP)
  - SkinEthic™ HCE eye irritation assays
  - HET-CAM
  - Investigational and mechanistic

With an integrated approach to ophthalmology research, Charles River has critical understanding of ocular diseases and the technical ability to guide our clients through the development process as efficiently as possible. Covering therapies of all types and implantable devices intended for management of ocular conditions, we can conduct stand-alone efficacy and safety studies, as well as general and specialty toxicology programs. Non-GLP pilot or proof-of-concept studies are available for early research needs, as is a wide variety of rodent and nonrodent animal models of ocular disease.

Efficacy & Safety Assessment Testing Services

Intraocular dosing presents a unique set of challenges across the various species used in research. Critical background knowledge of interspecies differences in ocular anatomy/physiology and specialized training in microsurgical techniques are essential. Small drug volumes and even smaller targeted delivery sites make intraocular dosing technically challenging; however, our team of ARVO- and board-certified veterinary ophthalmologists, trained veterinarians, and ocular research scientists have developed an industry-leading skill set to routinely perform these procedures with minimal complications.

Charles River has a complete suite of specialized diagnostic equipment required for detailed assessment of the ocular response to administration of novel compounds and devices. These include the Heidleberg Spectralis®, multimodel imaging, slit lamp biomicroscopy, indirect ophthalmoscopy, electroretinography, applanation/rebound tonometry, wide-field color fundus imaging, fluorescein/indocyanin green (ICG), optical coherence tomography, OCT angiography, confocal scanning laser ophthalmoscopy, specular microscopy, and corneal pachymetry. State-of-the-art operating microscopes, phacoemulsification/vitreoretinal towers, and a full complement of microsurgical instrumentation support both anterior and posterior segment surgical needs.

EVERY STEP OF THE WAY

Administration Routes

- Topical instillation
- Intravitreal/subretinal injections
- Subconjunctival/sub-Tenon's injections
- Intracameral injections
- Internal/external implants
- Transplants (corneal)
- *In vitro* (3D and bovine)

Pathology

Charles River has one of the most experienced ocular pathology teams in the contract research industry with the knowledge and expertise to perform specialized pathological assessments of ocular tissues within several key areas, including routine paraffin or cryo-sectioning, immunohistochemistry, and electron microscopy.

Immunohistochemistry methods allow for the visualization and morphometric analysis of cellular effects of ocular delivered compounds, expression of therapeutic transgenes or down-stream pathway constituents, and phenotype of implanted or transformed cells in ocular target tissues. These assays can be used to assess tissue responses to various treatments for proof-of-principle, efficacy, and safety evaluations. We offer a wide range of validated IHC markers/procedures and can develop custom study-specific labels.

With extensive experience in the field of electron microscopy, we offer full services with both transmission and scanning capabilities. We provide GLP-compliant transmission electron microscopy services for ultrastructural pathology. Scanning electron microscopy services provide additional topographic detail for the biocompatibility of device products, such as ophthalmic implants.

Laboratory Support Services

Our laboratory scientists use fully validated, networked data management systems at all laboratory locations for test article/item and sample management. We have made significant investments in highly trained chemists, facilities, and instrumentation to increase our capabilities and capacity to produce rapid and reliable quality data. Available services include formulation and analytical chemistry, bioanalysis (ELISA, HPLC, LC-MS/MS and capillary gel electrophoresis), immunology, and ocular tissue distribution (cold, radiolabeled (scintillation or QWBA) and fluorescent-labeled).

Polymerase chain reaction (PCR) is an extremely sensitive and specific technology that provides rapid quantitative results on the biodistribution and expression of transgenes, host cell DNA or RNA, or engrafted cellular therapeutics. Our GLP-compliant molecular pathology services (*in situ* hybridization and PCR-based evaluations) allow exact identification of cells in tissues. The integration of molecular biology and histopathology capabilities allows for the correlation of gene expression to tissue histomorphology, which provides valuable functional genomics information.

Regulatory Support

As with other types of pharmaceuticals, a battery of nonclinical studies is needed to support safety assessment of drug and device products administered via ocular routes. However, the regulatory expectations for these drug and products differ from those administered via systemic routes. Safety pharmacology studies are not generally needed due to low systemic exposure associated with ocular administration. In conjunction with our Scientific Advisory Services team, we can assist with the design of nonclinical programs needed to support the development of ocular drug and device products.