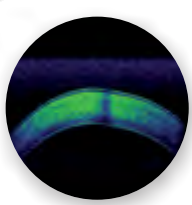
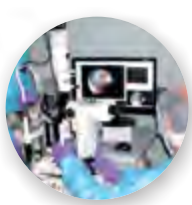
citoxlab
Safety and Health Research

Your partner for ocular drug discovery and development

www.citoxlab.com

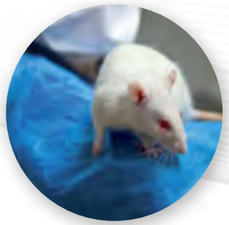
Your partner for ocular drug discovery and development

The assessment of ocular drug safety and efficacy has become more sophisticated with the advances of medical technology. Consequently, a greater range of therapeutic targets for ocular diseases (e.g. neurogenerative diseases, vascular disorders and age-related diseases) have become open to intervention.

Citoxlab is an industry leader in safety and efficacy assessments for ocular drug development. We have invested in valuable technologies such as electroretinography (ERG) and Optical Coherence Tomography (OCT), ophthalmoscopy along with other standardized and non-standardized non-invasive techniques used for interpreting changes in ocular structure and function *in vivo*.

In addition to a complete range of GLP ocular toxicology studies to support your regulatory submissions for ophthalmic drugs (including biologics and gene therapy) and medical devices. We also offer exploratory and ocular tolerability assessments.

At Citoxlab, ocular assessments, ocular imaging and ocular histopathology are performed by dedicated teams of veterinary ophthalmologists and histopathologists trained in the latest procedures in the field of ocular research. Our experts are committed to helping you achieve your ocular drug discovery and development goals.



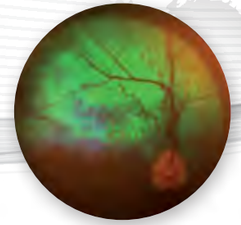
Species

- Rodent
- Rabbit
- Dog
- Minipig
- NHP

Routes of administration

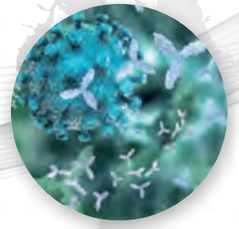
Includes, but not limited to:

- Intravitreal injection
- Anterior-chamber injection
- Sub conjonctival injection
- Topical ocular application



Ocular capabilities

- Ocular safety and efficacy assessments:
  - Range finding
  - Acute single dose toxicology
  - Subacute and chronic multi-dose toxicology
- Ocular structure evaluations
- Ocular function tests
- Ocular tissue biodistribution
- Ocular pharmacokinetics



Ocular test articles

- Small molecules
- Large molecules
  - Antibodies
  - Proteins
- Ocular implants
- Gene therapy / AAV
- Ocular devices

Specialized techniques

Available for safety assessments

- OCT (Spectralis OCT-2, Heidelberg Engineering)
- ERG (UTAS BigShot™, LKC Technology)
- Tonometry
- Esthesiometry
- Fundoscopy

Laboratory support

- Flow cytometry
- ELISA
- IHC and histopathology
- Efficacy, safety, and toxicity by Mass Spectrometry Imaging (MSI) applications for ophthalmic drug discovery with Imabiotech

Ophthalmic endpoints

Ocular observations

- Draize scoring test

Ophthalmic examinations

- Indirect ophthalmoscopy
- Slit-lamp evaluation
- Lacrimation/dry eye test (Schirmer test)

MacDonald and Shadduck (opacity) scoring method

- Post fluorescein staining of the cornea

Intraocular Pressure (IOP)

- Post administration of topical anesthetic

Electroretinogram (ERG)

- Light stimulus to evaluate the retinal function

Optical Coherence Tomography (OCT)

- Detailed tissue-morphology imaging of the eye at high resolution: Spectralis OCT-2

Ocular tissue analysis

- Pharmacokinetics: aqueous humor, vitreous fluids and tissue sub-compartments
- Histopathology: IHC and other staining techniques

Angiography

- Fluorescein and ICG available with set-up, upon request

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Safety and Health Research

TOXICOLOGY SERVICES

- General toxicology in all species
- Special toxicology
  - infusion, Inhalation, Dermal, Ocular
- Immunotoxicology
- Regenerative medicine
- Reproductive toxicology including minipigs and NHPs
- Carcinogenicity studies also in rasH2 and p53+/- mice
- Genetic toxicology: ICH compliant package
- *In vitro* toxicology: BCOP, h-CLAT, KeratinoSens™, DPRA, Photo 3T3-NRU, Episkin™, chicken eye test
- Agrochemical / chemical / REACH
- QSAR
- Physico-chemical testing
- Ecotoxicology: wide range of test species

SAFETY PHARMACOLOGY

- Integrated safety pharmacology in toxicology studies
  - CV (JET), BP
  - Respiratory (JET), plethysmography
  - CNS (FOB) and JET-EEG
- Safety pharmacology core battery
- *In vitro* assays
  - GLP compliant ion channel testing panel (hERG +5)
  - CNS *ex vivo* models for seizure liability screening
- Screening and follow-up models
  - Rodent and non-rodent LVP telemetry
  - Anesthetized models
  - Polysomnography
  - Gastrointestinal motility

DMPK, BIOANALYSIS, BIOMARKERS

- ^{14}C and ^{3}H ADME studies in all species
- *In vitro* metabolic clearance, metabolite ID and profiling, DDI package (metabolism and transporters)
- Bioanalysis: LC-MS/MS, GC-MS/MS, LC-ICP/MS, LC-Radiodetection, ELISA, RIA
- Toxicogenomics, miRNA: Affymetrix™ accredited service provider, next generation sequencing (Illumina®)
- Immunology: 10-color flow cytometer, Luminex, Meso Scale

MEDICAL DEVICE

- Biocompatibility testing
- Cardiovascular stents, electrophysiology and structural heart studies
- Long-bone defects and craniomaxillofacial/ dental models
- Spinal fusion models
- Joint and cartilage repair models
- Regenerative medicine (growth factors, biomaterials, cell and gene therapy)

SPECIALIZED EXPERTISE

- Juvenile studies including minipigs
- Ototoxicity in rats
- Fertility studies in rodents and NHPs
- Radiation safety and efficacy studies
- Drug transporter studies and Drug-Drug Interactions
- Tissue Cross Reactivity (TCR): human and animal tissue banks
- Gene therapy vector biodistribution via qPCR
- ES cell testing: devTOX™ and cardioTOX™ (with Stemina)
- Lead optimization and predictive toxicology services: Leadscreen™

aaalac INTERNATIONAL

GLP **CERTIFIED**

Citoxlab France
+33 2 32 29 26 26
contact.france@citoxlab.com

Citoxlab North America
+1 888 353 2240
contact.northamerica@citoxlab.com

Citoxlab USA / Xenometrics
+1 913 850 5000
info@xenometricsllc.com
www.xenometricsllc.com

AccelLAB
+1 450 435 9482
info@accellab.com
www.accellab.com

Citoxlab Denmark
+45 56 86 15 00
contact.scantox@citoxlab.com

Citoxlab Hungary
+36 88 545-300
contact.hungary@citoxlab.com

Atlanbio
+33 2 51 10 01 00
atlanbio@atlanbio.com
www.atlanbio.com

SOLVO Biotechnology
+36 62 424 729
sales@solvo.com - www.solvo.com

Media Services Ltd (Japan)
+81 3 3666 9915
citoxlab@mediaservices-jp.com

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