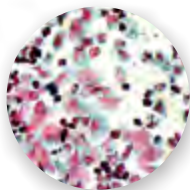


Your partner for  
developmental and reproductive toxicology



# Your partner for developmental and reproductive toxicology

Citoxlab offers GLP developmental and reproductive toxicology studies performed according to worldwide regulatory guidelines for safety testing of pharmaceuticals, biologics, gene-therapy products, food additives, chemicals, agrochemicals, veterinary medicines and consumer products. Studies cover the full scope of developmental and reproductive toxicology, evaluating potential effects on fertility, reproductive health, embryo-fetal, post-natal and juvenile stages of development, up to multi generation reproduction studies. Specialized evaluations can be combined in these studies, such as neurobehavioral testing, neuro-histomorphometry, sperm analysis, estrous cyclicity, developmental immunotoxicology, skeletal integrity, neurodevelopment and genomic analysis.

A comprehensive range of studies:

- Developmental and reproductive toxicology
- Juvenile toxicity studies
- Single and multi-generation studies



## Species

- Rodents
  - Mouse (CD-1)
  - Rat (SD, Wistar Han)
- Non-rodents
  - Rabbit (New Zealand White)
  - NHP
  - Gottingen minipig
  - Bird
  - Fish



## Broad experience in regulatory compliant study designs

- Fertility (ICH)
- Embryo-fetal development (ICH, VICH)
- Pre- and post natal development (ICH)
- Enhanced pre- and post-natal development in NHP (ICH, EMA, FDA)
- Developmental toxicity studies for vaccines (EMA, FDA)
- Developmental screening studies (OECD 421, 422)
- One or two generation studies (OECD 415, 416, 443)
- Developmental neurotoxicology (OECD 426)
- Juvenile toxicology (EMA, FDA)
- Customized designs/studies
- Uterotrophic assay (OECD 440) and Hershberger assay (OECD 441)



## Routes of administration

- Gavage (oral)
- Intravenous, including infusion (continuous or intermittent)
- Subcutaneous
- Intramuscular
- Dietary
- Inhalation
- Intranasal
- Dermal
- Intraperitoneal
- Rectal
- Vaginal
- Other: by Sponsor request



## Predictive developmental toxicology

- devTOX™ DISCOVERY (toxicity pathways)
- devTOX™ quick PREDICT (exposure-based)
- Stem cell-based models
- Low compound requirement
- Rapid turnaround
- Predictive, cost effective



## Minipig and NHP models

### Minipig:

- An alternative for DART studies:
  - Ease of synchronization of pregnancies facilitates optimal study design
  - Ever-expanding historical data available at Citoxlab and published for the minipig
- An alternative for embryo/fetal development and juvenile studies:
  - Sensitivity to human teratogens
  - Relatively large litter size
  - Short pregnancy period
  - Rapid development of piglets (entire juvenile period easily covered)
- Size of piglets permits:
  - All dosing routes from an early stage
  - Other investigations and assays: blood sampling, ECG, ophthalmoscopy

### NHP:

Developmental and reproductive toxicology testing in NHPs is being considered more often due to the increasing number of biopharmaceuticals in drug development. NHPs are frequently the only laboratory species to show pharmacologic similarities with humans i.e. the closest physiologically with less immunogenic response to:

- Humanized biopharmaceuticals
- Pediatric medicines
- Therapeutic monoclonal antibodies

Dedicated colony of mature, healthy, ready-quarantined Cynomolgus monkeys

## 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

- <sup>14</sup>C and <sup>3</sup>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™



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