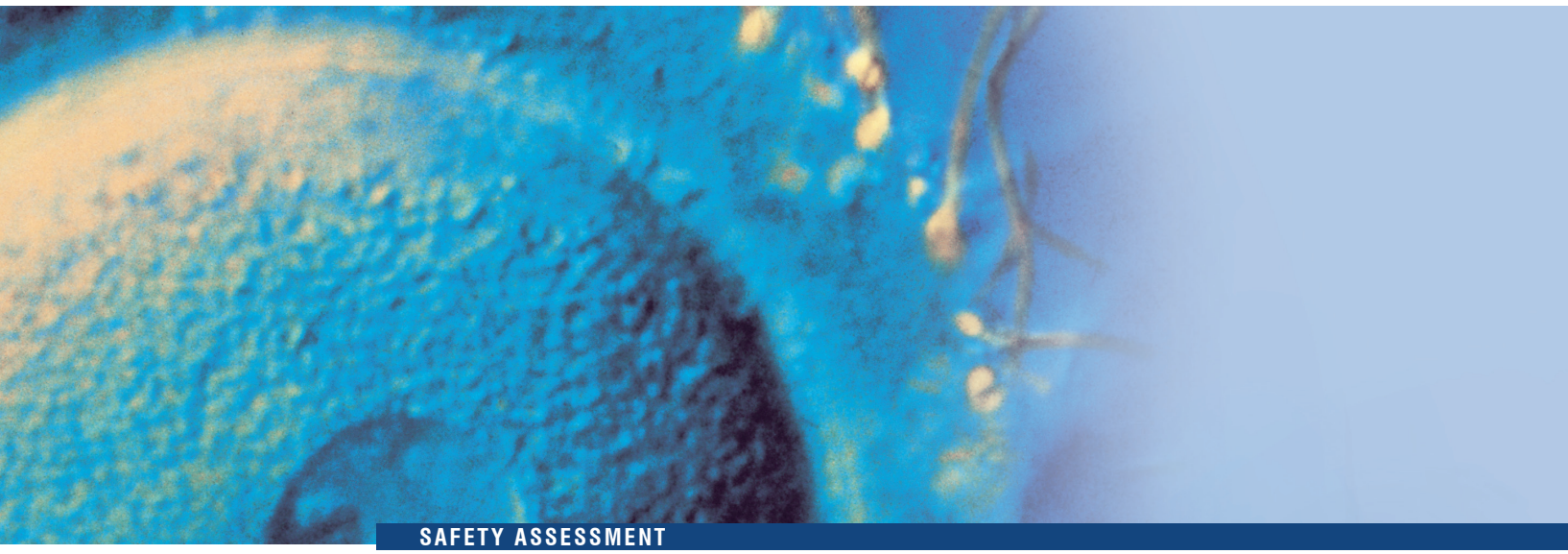
charles river



SAFETY ASSESSMENT

DART & Juvenile Toxicology Services

Comprehensive *in vivo* and non-mammalian services

Development and reproductive toxicology (DART) and juvenile toxicity studies in animals are integral parts of the nonclinical safety evaluation of drugs and hazard assessment of chemicals. The selection of an outsourcing partner is key to a product's success at this critical stage, and when a decision is based on program design, scientific depth, and data quality, many potential roadblocks to reaching key milestones can be avoided.

Charles River offers overall developmental and reproductive toxicology (DART), juvenile toxicity program planning, and individual study designs to conduct safety assessments for necessary products according to internationally recognized guidelines including ICH and OECD/EPA.

Charles River has the appropriate historical control databases and a highly experienced, global team of reproductive and juvenile toxicologists, widely published with many holding leadership positions in scientific societies including the Teratology Society, European Teratology Society, Middle Atlantic Reproduction and Teratology Association, Reproductive and Developmental Toxicology Specialty Section of SOT, and the American College of Toxicology.

Services:

- Formulation support
- Laboratory support
- Toxicology studies
- Specialty endpoints
- Pathology

EVERY STEP OF THE WAY

Formulation Support

Formulation development services range from pre-formulation investigations to analytical method development and validation. Charles River prepares formulations based on our extensive knowledge of vehicle suitability in animal models. We have experience with all of the standard formulation types including oral, parenteral, inhalation, and radiolabeled. Bulk test articles are analyzed to determine identity, purity, and stability to support GLP studies. Formulation analysis can also be undertaken to support toxicology studies.

Laboratory Support

Our team of scientists support both DART and juvenile toxicology studies with an integrated portfolio of services including bioanalysis, hormone analysis, clinical pathology, and immunology.

Bioanalysis

Our global bioanalytical laboratories use a range of techniques and technology platforms to ensure rapid lead-in times in order to meet critical deadlines. Our experienced scientists develop, validate, and apply quantitative methods to measure drug and metabolite concentrations for samples in plasma, serum, cerebrospinal fluid (CSF), urine, and tissue. Our comprehensive services can be performed on both small and large molecules, including antibody-drug conjugates, biosimilars, monoclonal antibodies, oligonucleotides, peptides, proteins, and vaccines.

Hormone Analysis

Our global bioanalytical laboratories also have the techniques and technology platforms to ensure rapid lead-in times in order to meet critical deadlines for hormone analysis. Our experienced scientists develop, validate, and apply quantitative methods to measure hormones in blood samples. Hormones measured include all steroid and peptide hormones, including inhibin and prolactin.

Clinical Pathology

Charles River offers a complete range of clinical pathology laboratory services to support preclinical studies. Our staff has extensive knowledge of animal and human hematology, coagulation, clinical biochemistry, and urinalysis. In addition, specialized pathology laboratory services are available to meet clients' assay or biomarker development needs for specific research requirements or drug safety studies. Our staff has expertise across the spectrum of major therapeutic areas and routinely assesses and interprets data from regulatory and investigative/research studies. With nine state-of-the-art clinical pathology labs, we can support all stages of human and veterinary drug development.

Immunology

Our comprehensive immunology, immunotoxicology, and immunogenicity testing supports our clients' preclinical programs for drugs and biologics. Our scientific, technical, and support staffs work together in dedicated immunology laboratories to conduct non-GLP and GLP/GCP immunotoxicology assessments. We conduct full method development/optimization, followed by validation and high-throughput sample analyses, which are performed in accordance with GLP regulations.

Developmental & Reproductive Toxicology Studies

We conduct male and female fertility, developmental toxicity (embryo-fetal development), pre- and postnatal development, multigenerational studies, and various mammalian specialty studies (e.g., endocrine disruption, thyroid hormone assessments, developmental neurotoxicity, and developmental immunotoxicity) and non-mammalian (zebrafish) studies to assess the potential effects of novel products on the entire reproductive spectrum. Our expertise includes pharmaceuticals, (including vaccines, biopharmaceuticals, and veterinary and medical devices) agrochemicals, industrial chemicals, and food additives. Our multigenerational study portfolio now includes the Extended One-Generation Reproductive Toxicity Study, required to satisfy OECD Guideline 443.

Juvenile Toxicology Studies

Charles River has successfully assisted in the designing and planning of appropriate neonatal and juvenile toxicology testing programs to support clients' registrations for pediatric use. The data from such studies is used to characterize risk for both efficacy and safety studies in the pediatric population. This experience, along with our extensive background data, enables us to undertake full product development programs for a diverse range of new chemical entities and biologics for pediatric use. These studies are supported by our extensive experience in behavioral testing, evaluation of bone development, immunology, and neuropathology.

Specialty Endpoints

We offer an extensive range of specialized endpoints to evaluate the effects on all organ systems, as well as reproductive functionality and skeletal growth. Behavioral endpoints are used to assess pre- and post-weaning behavior, including learning and memory, startle habituation, and locomotor activity. When required or desired, we can suggest and perform additional targeted assessments to extend a study's dataset including gravid telemetry measurement for blood pressure, postnatal skeletal development, cross-fostering studies, and various mechanistic studies.

Pathology

We offer a comprehensive support program for the implementation and evaluation of DART and juvenile toxicity studies that involve the assessment of male and/or female reproductive organs, as well as the assessment of sperm concentration, motility, and morphology. We are also able to perform stage-aware evaluation of spermatogenesis, and evaluation of thyroid follicular cell height and colloid area, as well as specialty endpoints such as neuropathology (including histomorphometry) and specialized skeletal densitometry.