charles river

SAFETY ASSESSMENT

REACH Services

The Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) regulation (EC) No 1907/2006 addresses the production and use of chemical substances, and their potential impact on both human health and the environment. Implemented on 1 June, 2007, the mandate created a single regulatory system for both existing and new chemicals in Europe.

Companies that had pre-registered their existing substances by the 1 December 2008 deadline were given a 10-year grace period to complete the process of achieving full registration. The 2018 deadline is fast approaching.

Under REACH, all chemicals manufactured or imported in quantities of greater than one metric tonne per annum must be registered in a central database managed by the new European Chemical Agency (ECHA) in Helsinki, Finland. ECHA handles the evaluation of dossiers and substances in conjunction with the member state competent authorities. Authorisation for use is required for substances of very high concern.

REACH puts greater responsibility on the industry to manage the risks from chemicals and to provide appropriate safety information. The legislation impacts all industry sectors and, ultimately, all downstream users of chemicals.

With over 40 years of experience in serving the needs of the chemical industry, the Charles River team is prepared to assist clients with meeting REACH requirements in a complete and timely manner.

Study Types:

- Physicochemical testing
- Acute toxicology
- Repeat-dose toxicology
- Carcinogenicity
- Reproductive toxicology
- Genetic toxicology
- Environmental sciences
- Ecotoxicology
- Analytical support
- Environmental fate
- *In vitro* studies
- Regulatory support

EVERY STEP OF THE WAY

Physicochemical Testing

Charles River conducts physicochemical testing with a wide range of chemical classes. Resulting data is proven to support registrations in the United States, Canada, Australia, South America, Asia and Europe. We help clients satisfy REACH requirements with a full range of testing services, available in complete packages or as stand-alone studies.

Available Physiochemical Tests:

- Physical state
- Melting point/freezing point
- Boiling point
- Relative density
- Surface tension
- Vapor pressure
- Water solubility
- Organic solvent solubility
- Octanol/water partition coefficient
- Dissociation constant
- Flammability
- pH
- Viscosity
- Oxidizing or reducing properties
- Hydrolysis as a function of pH
- Spectra (UV, UV/VB, IR, NMR, MS)

Toxicology

Charles River has extensive global capacity for all of our clients' rodent and reproductive toxicity testing needs. Our experience includes the accumulation of comprehensive background data, which is particularly relevant for supporting reproductive toxicology and carcinogenicity studies.

Acute Toxicology

Acute toxicity testing is used to define the intrinsic toxicity of a test item and provides data for establishing the risk assessment of acute exposure to a test item. We offer a full spectrum of regulatory-compliant studies to evaluate oral, dermal and inhalation toxicity, dermal and ocular irritation and skin sensitization. *In vitro* models are available to assess dermal irritation or corrosivity and ocular irritation.

Repeat-Dose Toxicology

Ranging from sub-acute to chronic exposure, we offer repeat-dose studies using standard and specialised routes of administration. All studies are supported by our formulation and analytical chemists and veterinary pathologists.

Carcinogenicity

Substances involving frequent or long-term exposure, and those shown to induce hyperplasia or pre-neoplastic lesions, often require additional data to illustrate their cancer causing potential. We conduct necessary carcinogenicity studies with a worldwide reputation for excellence in this field.

Developmental and Reproductive Toxicology (DART)

Our team of DART toxicologists is the largest in the industry, with vast experience in the design and conduct of reproductive toxicity studies to support international product registrations. We perform our studies in rodents and rabbits using appropriate routes of administration (e.g., oral, inhalation), and can include more specialized functional assessments such as neurobehavioral testing if required. Our complete portfolio of testing services includes the extended one-generation reproduction study, as well as reproductive and developmental screening. Our comprehensive historical control database is particularly relevant for supporting reproductive toxicology and carcinogenicity studies.

Genetic Toxicology

Our genetic toxicology studies typically follow a tiered approach, beginning with an *in vitro* (bacterial) Ames test and progressing to short-term *in vitro* assays using mammalian tissues. We offer a range of studies to include these as well as additional *in vivo* assays and alternative strategies such as the *in vitro* BlueScreen HC™ assay.

Environmental Sciences

Charles River offers a comprehensive range of environmental testing services, with specific expertise in handling volatile, complex, unstable or poorly soluble compounds.

Ecotoxicology

Our custom-designed ecotoxicology facilities enable both aquatic and terrestrial toxicology investigations. All of our laboratories have independent environmental controls to accommodate a wide range of test organisms and conditions, including radiolabeled test items.

Analytical Support

We have a dedicated team of analytical chemists who have many years of experience in the development and validation of methods intended for aqueous samples to support ecotoxicology studies. Working closely with our ecotoxicologists, they ensure that potential issues such as poor solubility and stability under test conditions are addressed as early as possible in the program.

Environmental Fate

Charles River uses environmentally controlled incubation rooms to conduct the in-life phases of environmental fate studies. Test systems are available from a wide variety of geographical locations globally. All are fully characterized and confirmed as viable before the start of the study.

In Vitro Absorption Studies

Under section 8.6.2 of the REACH guidelines, the requirement for a sub-chronic toxicity study in rodents can be determined by conducting an *in vitro* dermal absorption study. We routinely perform studies that are designed to comply with OECD Test Guideline 428 in conjunction with the accompanying Guidance Document No. 28, as well as other relevant industry documentation.

In Vitro Corrosivity and Irritation Models

We offer two *in vitro* models created by SkinEthic as alternative methods to screen for dermal/ocular irritation and corrosive potential (OECD 431 and 439). The SkinEthic models are 3D reconstructed human epidermis (EpiSkin®) and human corneal epithelium (HCE) that provide accurate data while eliminating the need for animals. The models have undergone ECVAM pre-validation as a potential alternative to OECD 405.

MucilAir™ *In Vitro* Human Airway Toxicity Test

MucilAir™ is a mucus secreting, ciliated epithelial model of the human airway produced by Epithelix Sàrl, Switzerland. It is derived from human airway cells that have been collected from healthy donors and cultured at the air interface on permeable membranes. We offer this as an *in vitro* model with morphology and functions mirroring the tracheobronchial epithelium which can be used to identify potential airway toxicants in chemicals.

Regulatory Support

Our advisory services include the assessment of data requirements, data evaluation, and dossier preparation. For non-EU manufacturers, we can serve as sole representative, and for importers or EU manufacturers, we can act as a third-party representative.