charles river

SAFETY ASSESSMENT

Veterinary Pharmaceutical Development

Integrated services for development and global registration

Achieving your milestones is highly dependent on good communication, minimizing technical deviations and satisfying regulatory expectations. Having a development partner with an integrated network of experienced scientific staff who have been troubleshooting unexpected toxicity or other issues as a team for many years, will greatly benefit your products' development timeline.

Scientific and technical experience on individual elements of the program that is easily shared between different teams means that issues are quickly communicated and resolved. Staying one step ahead of the constantly changing regulatory landscape makes it easier to dedicate the appropriate resources and ensure compliance. Charles River has been serving the testing and regulatory needs of the veterinary pharmaceutical industry for more than 40 years, offering the full range of integrated services to support development and international registration of veterinary medicines.

Our flexible approach to the design of development programs helps our clients meet the registration needs of new products and provides support for maintenance of existing marketed products in all major markets. Our expert scientists are specialized in the design of studies to satisfy the requirements of the various authorities in Europe, the US and Japan. In addition to satisfying quality assurance standards (GLP, GCP), we perform all studies in accordance with international guidelines (EMEA, FDA-CVM, VICH, etc.). Our regulatory support includes exposure and safety assessments required in the different parts of the dossier.

Areas of Expertise Include:

- Analytical Capabilities
- Bioanalysis
- Studies in Target Animals
- Clinical Trials
- Toxicology
- Environmental Sciences
- Biosafety Testing
- Market Authorization/Regulatory Support

EVERY STEP OF THE WAY

We have comprehensive laboratory and animal services for preclinical work. This includes the full range of studies from mammalian toxicology, chemistry, pharmacokinetics and environmental studies through veterinary metabolism and residue studies. A large range of in vitro and in vivo studies can be managed using non-radiolabeled or radiolabeled analytical methods. Clinical studies are conducted either at our veterinary clinical facility in the UK or monitored from the UK and conducted worldwide.

Analytical Capabilities

Charles River has experience with traditional chemical as well as new biological entities. We also routinely work with products prepared as solutions, suspensions, solid dosage forms, aerosols, feed additives and sterile parenterals.

Dose Formulation

Test items can be formulated into the test solution/suspension, diet or capsule prior to dosing. The analytical methods used to support toxicology programs commonly involve liquid or gas chromatography (HPLC or GC); a selection of detector types is available for each technique to suit the nature of the test item. A variety of other analytical techniques (e.g., mass spectrometry) is also available to ensure that sensitivity and specificity requirements are met.

Physicochemical Characterization

Charles River has vast experience conducting various physicochemical testing packages (or stand-alone tests) to assess the environmental impact, quality and safety of the active ingredient and its formulated products. We offer a full range of physicochemical testing to meet all regulatory requirements, such as OECD and OCSPP.

Stability Testing

Charles River also performs characterization and stability studies for new drug test items and products. We provide a full service in analytical development and validation, in combination with real-time and accelerated storage stability testing.

Bioanalysis

Charles River provides routine and specialized bioanalytical services supporting discovery through preclinical to clinical trials. Our scientists can develop and validate quantitative bioanalytical assays from first principles or, alternatively, transfer a method from a client's laboratory. Our comprehensive services can be performed on a wide range of veterinary therapies, including vaccines.

Studies in Target Animals

Charles River has over 40 years of experience in conducting the many different types of studies in target animals in compliance with the EU, US and Japanese regulations and according to the VICH guidelines. Our portfolio is comprised of target animal safety, drug metabolism, residue studies, bioequivalence, reproduction, dose determination/confirmation and palatability studies.

Target Animal Safety

Our scientists can design tolerance studies in target animals to meet specific requirements for regulatory submission. We work with all common livestock and domestic pet species, and are experienced in using all types of formulations and routes of administration. We are unique in being able to offer all the necessary support services (clinical pathology, histopathology, statistical analysis) for these study types.

Metabolism Investigations

In vitro and *in vivo* metabolism studies are conducted using radiolabeled test items in a wide variety of laboratory and target animal species. In addition, we routinely process, characterize and identify metabolites and degradation products from edible tissues and excreta and, when required, quantify. The majority of our studies are carried out in accordance with VICH guidelines and in compliance with the US Food and Drug Administration as well as the European regulatory authorities.

Residue Studies

Residue studies can be conducted in all food-producing animals for worldwide registration. We have experience in the conduct of residue studies with either radiolabeled or non-radiolabeled test items. We can also identify the marker residue, where this is initially unknown.

Pharmacokinetics and Bioequivalence

In vitro and *in vivo* pharmacokinetics studies can be managed for screening or regulatory studies. Pharmacokinetic studies can be performed to define pharmacokinetic behavior of novel test items or formulations, or to demonstrate bioequivalence for generic products. We have worked with all typical dose routes in the full range of target species, and can design and execute studies to meet current international guidelines.

Clinical Trials

Charles River also conducts single and multi-site clinical trials. Our research farm in Scotland has over 50 hectares of grazing and more than 5,000 square meters of large animal accommodation. Multi-site field efficacy and field safety clinical trials can be carried out throughout Europe in livestock, poultry and domestic pet species. Veterinary clinical studies are run in accordance with VICH GCPv guidelines and are supported by our in-house Quality Assurance and Statistics teams.

Toxicology

We offer a full spectrum of *in vitro* and *in vivo* short- and long-term toxicology studies to evaluate oral, dermal and inhalation toxicity, dermal and ocular irritation and skin sensitization. We also perform neurotoxicology (detailed functional observations and assessments), immunotoxicity studies and have more than 25 years' experience conducting a wide range of genetic toxicology assays.

Reproductive Toxicology

Reproductive toxicology is a highly specialized discipline that plays an important role in the safety evaluation of pharmaceuticals. We offer a full portfolio of reproduction, teratogenicity and peri- and postnatal studies to assess the potential detrimental effects of test items on the reproductive process. All of our reproductive toxicology work is supported by the largest historical control database in the industry.

Pathology

Understanding toxicologic pathology is a key component of drug safety evaluation. Our scientists provide clinical pathology as well as postmortem necropsy and histopathology services with experience in a wide range of animal species and techniques. Histopathological evaluation and scientific interpretation are performed by highly specialized veterinary pathologists. Cutting edge analytical techniques are also available to further investigate toxic mechanisms and to study biomarkers.

Environmental Sciences

Many animal health products may enter the aquatic and terrestrial environment through excretion; therefore, the potential environmental impact associated with their use must be assessed. The environmental scientists at Charles River are experienced in the conduct of studies required to identify and manage the environmental risk of veterinary pharmaceuticals. They can advise the design of individual studies as well as complete programs, and have particular expertise in developing single studies which satisfy the requirements of more than one regulatory authority.

Ecotoxicology

Aquatic tests are conducted under static, semi-static (renewal) and flow-through conditions. Our scientists have experience with the full range of regulatory study species, including cold- and warm-water fish, *Daphnia magna*, algae (freshwater and marine), *Lemna* spp. and *Chironomus riparius*. Studies are also undertaken to determine toxicity to terrestrial organisms and beneficial insects including phytotoxicity tests in terrestrial crop and non-crop species to determine effects on seed germination, seedling emergence and vegetative vigor, earthworms and soil microbes. We are experienced in handling difficult test items (e.g., volatile, unstable or partially soluble) and have the facilities and equipment to deal with these complex test situations. If necessary, any particular test can be conducted with a radiolabeled test item.

Environmental Fate

Our modern laboratory facilities are equipped to support a wide range of environmental fate and related studies. Studies can be conducted to assess aerobic and anaerobic degradation in soils and sediment waters, aerobic mineralization in surface waters, degradation in manure and slurry, as well as ready and inherent biodegradation and soil or sludge adsorption, desorption and mobility investigations. We can perform hydrolytic stability and accelerated hydrolysis as well as photolytic degradation in both moist and dry soil surfaces and aqueous systems.

Biosafety Testing

Charles River provides the services required to conduct an expert assessment of the potential risk of biologically-derived animal health products. The key elements in a biosafety testing program include detection of adventitious agents, removal and/or inactivation of adventitious agents, characterization and stability of the product and, where appropriate, the cell line.

Market Authorization/Regulatory Support

Charles River provides regulatory support for full or abridged applications as well as for variations, extensions and renewals. This includes pre-submission support, preparation and submission of dossier, and post-submission and post-authorization support. Our regulatory expertise covers scoping, scientific advice on testing strategies, data gap analysis, study monitoring, dossier compilation including exposure and risk assessment discussions with respective authorities, etc. Our experts take into account the product's specific use (e.g., duration) and target species when determining the testing and regulatory strategy.

We can also prepare specific MRL dossiers as well as environmental impact assessments, benefit-risk assessments and periodic safety update reports for veterinary products.