Minipig Toxicology

The minipig is becoming more frequently selected as the nonrodent species in pharmaceutical development programs due to its physiological similarity to humans (skin structure, digestive, cardiovascular and urinary systems), ready availability, known disease status, and ability to be genetically and phenotypically controlled. As such, regulatory authorities now accept the minipig as a suitable nonrodent species for use in safety evaluation assessment and efficacy studies of pharmaceutical products when scientifically appropriate.

Global Expertise
Charles River has been performing toxicology studies in minipigs for over 30 years. We currently offer minipig programs at three locations throughout North America and Europe, giving you the opportunity to choose a site based on location and capacity. All of our sites are equipped with the most advanced technologies, and our experienced and expert staff members provide the knowledge and resources you need to make better development decisions and guide your lead compounds forward in the development process. Our experts are experienced in running a wide range of study types in multiple minipig strains (most commonly the Göttingen minipig) and are available to advise on study design. We also offer full-service laboratory support to enable each client to have all aspects of a study performed at a single GLP-compliant facility.

Intravenous Administration
Intravenous administration can be performed as bolus injections via ear vein or implanted catheter, or as intravenous infusions using cannulated methods for continuous or intermittent infusion regimens for up to 6 months. Cannulated methods typically utilize cannulation of the vena cava, performed with entry via the femoral vein (a procedure comparable to that used in rodent and other nonrodent species). While the cannula is in place, continuous saline infusion is used to maintain patency (no anticoagulant is used) and historical background has shown infection rates maintained at < 1%.
Subcutaneous Administration
Subcutaneous administration can be performed as injections or infusions using a temporary indwelling cannula and rotation of sites. This model may be of marked interest for evaluation of the irritancy potential of formulations intended for subcutaneous administration. In particular, it allows for evaluation of reactions from the epidermis to the subcutis following single administrations at various levels/sites, or repeat administrations at given site(s) within the same animal to mimic or surpass the clinical plan.

Dermal Administration
Dermal administration typically uses the dorsal surface. Compared to other large animal species, the skin of the minipig more closely resembles that of the human in many respects, including sparse distribution of the hair coat, overall histologic appearance, epidermal thickness, keratinocyte turnover time, xenobiotic metabolic activity and similar dermal penetration rates for many chemicals. The applications can be occluded/non-occluded, utilizing wrapping materials and rinsing procedures with exposure times of up to 24 hours or multiple times daily. A standard dermal grading based on the Draize scoring system is a standard study element.

Ocular Research
Of the species used for ocular safety evaluations, the minipig's eye most closely approximates the size of the human eye. The minipig also has similar innervation and vascular structure to humans, making it one of the most suitable eyes for intraocular administration in preclinical ocular toxicity studies. With over 20 years of experience in ocular safety evaluation, Charles River is uniquely positioned to tailor ocular studies and product development programs in this challenging species. Small molecules, biologics, gene therapy and cell-based therapy have all been evaluated in minipig eyes at Charles River. The larger eye size permits the implantation of clinical devices and conduct of clinically relevant surgical procedures and facilitates translation of preclinical results to the development and support of clinical protocols.

Safety Pharmacology
We also are capable of conducting safety pharmacology studies using the minipig. Note, the safety pharmacology core battery requirements for the assessment of effects of substances on the cardiovascular system (per the ICH S7A requirements and S7B guideline) are limited to assessments of heart rate, systemic blood pressures and quantitative and qualitative analysis of the electrocardiogram (ECG).

The majority of cardiovascular studies are performed using radiotelemetry-based systems, since these provide high-quality, continuous data from conscious, freely-moving animals. A standard single pressure telemetry device with ECG capability allows cannulation of the lower femoral artery to provide a direct measurement of blood pressures, and placement of subcutaneous or epicardiac ECG leads in a Lead II configuration provides a continuous ECG signal. An additional dual pressure telemetry device can be used, whereby the second catheter is placed into the left ventricle for assessment of contractility and left ventricular pressure. The important advantage of telemetry-based systems is the ability to collect continuous data over long periods of time, and to analyze this in a real-time environment. Data are immediately available to guide dosing within a study and allow quick decisions on the direction of compound development.

An Alternative Approach
The use of the minipig as an alternate nonrodent species has been well documented and was recently the subject of the RETHINK European FP6 project. The RETHINK project evaluated the potential impact of toxicity testing in the minipig and established the use of this species as a valid alternative approach in regulatory toxicity testing that can contribute to the replacement, refinement and reduction of animal testing (3Rs).