charles river

**Summary**

From the in-life phase through analysis, Charles River performs an average of 10 livestock metabolism studies per year, providing clients with a proven, cost-effective solution for satisfying this complex regulatory requirement.

SAFETY ASSESSMENT

# Livestock Metabolism Studies

## Agrochemical Product Development

Charles River routinely conducts studies to OECD 503 or US EPA 860.1300. Our facilities are specifically designed to house all common livestock species. While lactating ruminant (goat or cow) and poultry studies are routine, we can accommodate other species when metabolism data from a third food-producing species is required.

Our dose formulation experience is diverse, ranging from aquatic-based solutions to oil-based suspensions.

We also offer a complete supporting radiochemistry and analytical service portfolio:

- Management of radio-synthetic chemistry
- Radiolabeled dose formulation and stability
- Laboratories designed for the analysis of commodities from any species
- Extraction and analytical techniques tailored to the nature of the test article and commodity
- Advanced chromatography and mass spectrometry systems used to quantify and identify metabolites
- Collaboration with chemists conducting plant metabolism, environmental fate and rat biotransformation studies
- Available synthetic chemistry services for the preparation of reference standards

### In-Life Phase

In-life phase animals are dosed orally until plateau is established in milk or eggs. Dose capsules are prepared based on food consumption during acclimatization. Excreta are collected daily and milk or eggs collected twice daily. Animals are sacrificed between 6 and 12 h post-final dose, depending on the rate of absorption and excretion or PK data. Edible tissues are collected and assayed for total radioactive residues. Non-food commodity samples (e.g., bile, blood, GI tract) are also collected to aid metabolite identification and for mass balance purposes.

Radioactivity in milk is separated into fat- and water-soluble fractions. Egg yolks and whites are assayed separately for total radioactivity and total radioactive residue is reconstructed from those data. Mass balance data are based on radioactivity in excreta, milk/eggs, GI tract and tissues. The total dose in muscle and fat may be estimated based on literature calculations if residues in these commodities are high. Dose stability analysis is performed on capsules and on dose formulation using radio-HPLC.

## Analytical Phase

Composite samples for each tissue type can be prepared or samples can be extracted and analyzed individually. Extraction and analytical techniques are designed to achieve an LOQ of at least 0.001 mg equiv/kg. Multi-step extraction procedures are tailored to the nature of the test item and tissue type. Enzyme deconjugation can be used to characterize Phase II metabolites. Radioactive residues in solvent extracts are quantified using either radio-HPLC or TLC with phosphor imaging. HPLC radiochemical detection is by ß-Ram using Laura Version 4 software. TLC autoradiograms are obtained using a Fuji FLA5000 Bioimaging device and Aida software. Non-solvent extractable residues are further investigated using enzymes and surfactants.

Significant metabolites in tissues and excreta are identified using state-of-the-art mass spectrometry technology. Our Edinburgh facility uses high-resolution Shimadzu Ion Trap/Time-of-Flight (Shimadzu IT-TOF), Waters SYNAPT G2-S and Waters Q-TOF instruments. Typically, accurate mass error of less than 5 ppm is achieved for both instruments. High sensitivity triple quadrupole LC-MS/MS (Applied BioSystems API 5000™) systems are also used.