SEKISUI XENOTECH

Sekisui XenoTech provides in-vivo ADME services to support IND-enabling projects

Sekisui XenoTech offers *in vivo* ADME services through its parent company, Sekisui. Sekisui's *in vivo* team boasts over 45 years of experience and routinely perform over 200 studies per year. Sekisui Medical Company's Drug Development Solutions Center is located in Tokai, Japan. This campus features almost 150,000 ft^2, consisting of corporate and administrative offices and research laboratories on 8.42 acres. Laboratories include two clean rooms for cell culture, an animal care facility and a large variety of instrumentation to support both radio-labeled and unlabeled investigations for *in vivo* and *in vitro* ADME/Tox studies. Sekisui offers comprehensive services in Absorption, Distribution, Metabolism and Excretion (ADME) studies to support IND-enabling projects.

Drug Development Solutions Center, Tokai, Ibaraki, Japan

Equipment and Capacity

- Full AAALAC Accredidation
- 13 Liquid Scintillation Counters
- 1 γ counter
- 16 Radiometric Flow Scintillation Analyzers
- 3 Bioimaging Analyzers
- 4 Liquid Handling Workstations
- 15 LC-MS/MS Systems (API 4000, 5000 & QTRAP 4000, 5500)
- 2 LTQ-Orbitraps
- 2 Real-Time PCR Systems
- 2 Genetic Analyzers
- 1 Nuclear Magnetic Resonance Spectrometer
- 3 Microtomes (Leica)
- 1 SECTOR Imager 6000
- 1 Bio-Plex immunoassay system
- 1 Digital ELISA system (Simoa HD-1 analyzer)

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Isotopes

^{14}C, ^{3}H, ^{125}I, ^{111}In, ^{33}S, ^{35}S, ^{90}Y

Species

Mouse (600), rat (320), guinea pig (288), marmoset (8), rabbit (96), dog (54), minipig (5), Cynomolgus and Rhesus monkey (32). Knockout mouse and rat models also available. *Facility capacities (# of animals) are noted in parentheses.*

Administration

Single and multiple dosing

Administration routes

Oral, intravenous, continuous intravenous, transdermal, subcutaneous, intramuscular, intratracheal, instillation, intrarectal and intraduodenal

Study Capabilities

Absorption

- Drug plasma concentration
- Absorption site investigation

Distribution

- Tissue distributions (over 30 organs)
- QWBA (Quantitative Whole Body Autoradiography)
- Micro-autoradiography
- Plasma protein binding
- Blood/plasma partition rate
- Placental transfer

Metabolism

- Metabolite analytical method set-up
- Metabolic profile (plasma, urine, bile and tissues)
- Metabolite identification

Excretion

- Excretion rate (urine, feces, expiration air and bile)
- Enterohepatic circulation
- Lymphatic partition rate
- Excretion into milk

PK Study (using unlabeled test compound)

- Development of measurement system, administration, sample collection and sample measurement

Additional options available:

- Prediction of human metabolites using chimeric mice with human hepatocytes
- Custom RI synthesis
- Purification of labeled compound
- Customized report
- Biomarker measurement

Contact us to learn more about our *in vivo* capabilities:

1101 W Cambridge Cir Dr | Kansas City, KS 66103 | *p* (877) 588-7530 / +913.438.7450 | *f* (913) 227-7100 | xenotech.com | info@xenotechllc.com

Together, Sekisui XenoTech offers full radio-labeled synthesis capabilities.

Knowledge of the pharmacological effects of an investigational drug in the human body at an early stage has become increasingly necessary to avoid costly-late stage clinical trial failures.

To evaluate the performance of a potential drug earlier in the development cycle, usually in Phase I, and to reduce financial risk, industry is now increasingly conducting ADME studies in humans. This is accomplished by placing a radioactive tag at a metabolically stable site of an investigational drug. This tag makes it possible to study the drug's disposition and allows for the identification of metabolites (detection of structurally unidentified metabolites). The use of radio-labeled compound allows drug developers to make informed decisions about committing resources to the development of a chemical entity for commercial application.

Together with Sekisui (formerly Daiichi Pure Chemical), Sekisui XenoTech offers the following radio-labeled synthesis services:

- ^{14}C- & ^{3}H-labeled compound synthesis
- ^{14}C-fermentation
- ^{3}H, ^{125}I, ^{111}In, ^{33}S, ^{35}S, ^{90}Y protein and peptide labeling
- Re-purification and stability analysis
- Storage/re-analysis

About Sekisui

Our parent company, Sekisui Medical, has over 50 years experience synthesizing radio-labeled compounds. Sekisui adheres to a quality management system to assure the highest quality labeled compounds while meeting strict customer requirements. Sekisui employ radio chemists specializing in complicated and long-step radio-synthetic sequences. ADME studies and radio synthesis are performed at the the same facility, allowing seamless execution of pre-clinical and *in vivo* ADME/Tox studies.

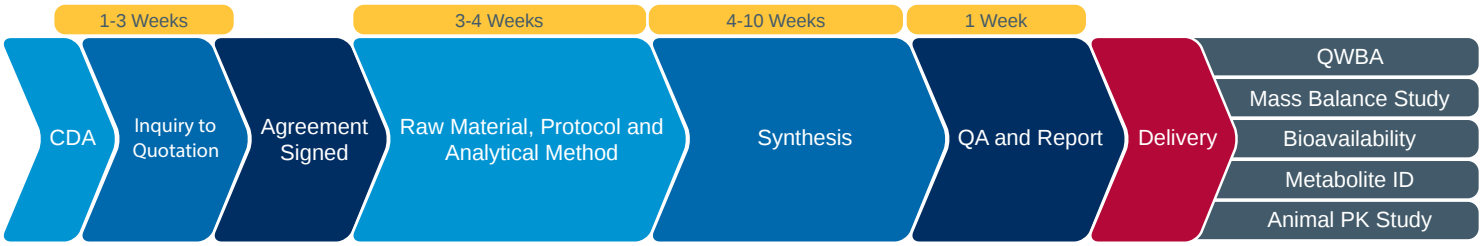
Why Sekisui?

- *Compliance* – Protection of confidentiality and intellectual information
- *Strict Quality Control* – Certificate of Analysis issued for each compound synthesized and a full report for GLP-compliant services
- *Experience* – Over 50 years of experience, employing the most experienced radiochemists to consult on appropriate label position, isotope species, radioactivity, etc.
- *Additional ADME & Tox studies available at the same facility*
  - Animal *in vivo* studies: QWBA, Mass Balance, Bioavailability, Metabolite ID and PK studies
  - Covalent Binding, Radio Immuno Assay (RIA), Radio Receptor Assay (RRA) and Micro Auto Radiography (microARG) studies
  - Microdose studies
- *Partnerships* – Global partnerships allow for expanded capabilities and selection to ensure cost effective options
- *Project Management* – Studies are managed by XenoTech. Client does not need to be involved in the daily management.

From Inquiry to Completed Study, What to Expect

Sekisui XenoTech will consult with the client on the desired specifications to provide the desired deliverable. Topics to discuss include:

- Synthetic route and yield at each step
- Compound name and structure (isomers)
- Labeling position
- Radioactivity required (mCi or MBq)
- Specific activity (mCi/mmol)
- Radiochemical purity
- Chemical purity
- Target delivery date



Timeline represents a typical synthesis but actual time may vary depending on the number of synthesis steps.

Contact us to learn more at **www.xenotech.com** or call **913.438.7450**

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