



Member of  **GBA** GROUP



In-Vivo, Ex-Vivo & In-Vitro Liver related ADME Toxicology Studies



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***In-vitro* screening for CYP induction**

- Exposure of plated cryopreserved hepatocytes (human, monkey, dog, minipig, rat and mouse)
- mRNA expression by RT-qPCR

***In-vitro* regulatory (FDA/EMA) CYP and UGT induction**

- Exposure of plated human hepatocytes (from 3 donors), pre-characterized for response to positive control inducers, including for CYP Relative Induction Score

***In-vitro* metabolic Stability & Metabolite Identification**

- Exposure of plated hepatocytes from various species, and incubated for several days, up to 7 days, in a sandwich culture configuration allowing long-term culture and incubation
- Measuring at multiple time-points the concentration of parent compound and metabolites with the help of HPLC/MS*

***performed by Pharmacelsus**

***In-vitro* and *Ex-vivo* Drug Induced Liver Injury**

- Cell viability
- Oxidative Stress
- Steatosis
- Cholestasis

***In-vitro* and *Ex-vivo* Acute and Chronic Liver-related Toxicities**

- Induction, repression or inhibition of major liver metabolic enzymes,
 - *ex-vivo* in liver samples from animals of toxicology studies
 - *in-vitro* from plated hepatocytes of various species, and exposed for several days, up to 7 days, in a sandwich culture configuration allowing long-term culture and incubation
- Cell Proliferation
- Using RT-qPCR for gene expression and LC-MS* detection for enzyme activities

***performed by Pharmacelsus**

Others

- *In-vitro* assays for evaluation of direct effects on thyroid (TPO, DEIO, NIS)

Bioanalytic

- Quantifying compounds and their metabolites in wide range of sample types for several compound classes

Biomarkers

- Multiplex high-throughput detection, quantification and characterization of Biomarkers (cytokines, hormones, enzymes)

***In-vivo* Toxicokinetic Studies**

- Acute, Chronic und Subacute Studies (Dose range finding and Maximum Tolerated Dose Study)

Tests for Immunotoxicity in Conjunction with PK Studies

Checking for immunosuppression and Immunogenicity

- Immune Phenotyping of treated Animals
- Detection and quantification of Biomarkers
- Histamine Release

Metabolite Identification in conjunction with PK Studies

- Identification of newly formed metabolites in Blood, Plasma, Urine, Faeces, Tissues
- Structural Elucidation of Metabolic Modification

***In-vitro* ADMET Program**

A bsorption	Physico-Chemical Parameters, Stability, Membrane Permeability, Transport, Protein Binding
D istribution	
M etabolism	Drug Interaction, Metabolism, Clearance
E xcretion	
T oxicity	Cytotoxicity Testing



About Kalycell

KaLy-Cell has been developing its expertise in liver-related ADME-toxicology, ex-vivo and particularly in-vitro with hepatocytes, for almost 20 years, helping in optimizing the discovery, development and approval of drugs, food additives, agrochemicals and nutraceuticals.

KaLy-Cell delivers unique informations, mainly with hepatocytes, from animal and human origin, qualified in short- and long-term culture, to best support evaluation of drug efficacy, xenobiotic safety, and to explain mode of actions and adverse reactions.

About Pharmacelsus

Pharmacelsus, Germany's market-leading early stage CRO, plans, organizes and realizes customized preclinical studies for more than 20 years. Predicting the in-vivo pharmacokinetic, pharmacodynamic and toxicity (both in-vitro and in-vivo) characteristics of new chemical entities plays an important role on the way to drug discovery and development.

Pharmacelsus supports entire process of preclinical drug development in order to perform Early Safety de-Risking and help you to choose the most suitable candidate for clinical trials. All the assays are performed in quality-controlled way, GLP studies are possible.

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Your Benefits

- Flexible study plan and timelines
- *In-vitro* long-term toxicity and DMPK assessment in various species including human
- Short- and long-term (slow metabolizer) metabolic assessment with or w/o MetID in Hepatocytes in various species
- Metabolic stability and DDI assays with or w/o metabolite profiling
- Assay performance and Bioanalytical read outs