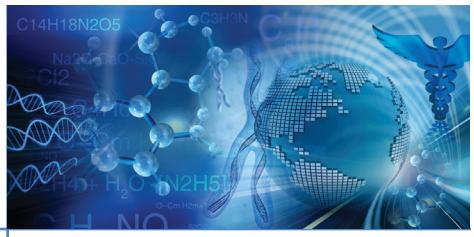
BioReliance

Toxicology Services



Mass Spectrometry Services

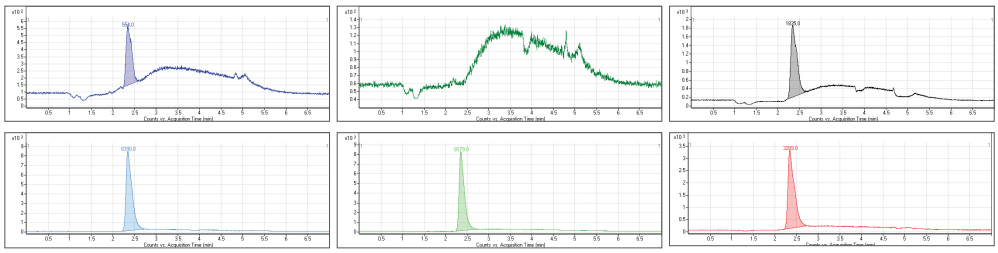
Introduction

BioReliance offers a fully validated, state-of-the-art GLP analytical service using Liquid Chromatography–Mass Spectrometry (LC/MS). This powerful technology provides quantitative analysis of chemicals within a given sample, with high sensitivity and selectivity. In addition to its application as a more sensitive analytical process, LC/MS is employed for toxicokinetic (TK) studies.

As an innovator in Toxicology, BioReliance has long offered animal studies to identify genotoxic hazard and carcinogenic risk. Now with the introduction of LC/MS and TK capabilities, BioReliance provides full in vivo studies, evaluations and analytical chemistry under the same roof.

Technology

BioReliance employs the Agilent 1200 LC System with the Agilent 6430 Triple Quadrupole LC/MS System for fast, dynamic and sensitive chemical analysis. This system has 400 bar pressure (up to 5 mL/min) for fast separations, 30 ms polarity switching for fast peaks, 1 ms dwell times for analyzing hundreds of compounds, dynamic MRM methods for analyzing thousands of ion transitions, and detection of molecules up to 3,000 Daltons; making it ideal for high pressure liquid chromatography (HPLC) separations. The combination of these two compatible systems allows for true LC/MS/MS analysis. This system is also equipped with MassHunter software, which allows for fully automated and streamlined MS evaluation, from instrument tuning through final analysis, creating dynamic and reliable reports.



Toxicokinetics

On March 1, 1995 the ICH S3A Guideline entitled, "Toxicokinetics: The Assessment of Systemic Exposure in Toxicity Studies for Industry" was published in the Federal Register (60 FR 11264). This guideline was developed within the Expert Working Group (Safety) of the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) and is applicable to drug and biological products. In this guidance, toxicokinetics is defined as "the generation of pharmacokinetic data, either as an integral component in the conduct of nonclinical toxicity studies or in specially designed supportive studies, in order to assess systemic exposure." Thus the bioanalysis data provided in a TK study may be used in the interpretation of toxicology findings and their relevance to clinical safety issues, as well as to establish that appropriate dose levels have been achieved in nonclinical assays. TK data are an integral part of any nonclinical testing program and recommended in conjunction with in vivo toxicity studies.

BioReliance provides a complete TK testing program to accompany animal studies performed in our facilities, or to support studies performed elsewhere. See back for parameters available through our TK platform.

Analytical Chemistry

In addition to our HPLC capabilities, BioReliance can now perform basic chemical analyses with the dynamic and sensitive LC/MS/MS technology. These analyses include: analytical method validation, dosing matrix analysis, and stability analysis. BioReliance can transfer any existing analytical method or develop its own to meet client needs. We can also perform analysis of the stability of test articles and dosing formulation verification for any of our Genetic Toxicology or Mammalian Toxicology assays and protocols. See back for specific analyses available.

State-of-the-Art Technology for Toxicokinetics and Standard Analytical Chemistry

Fully Validated, GLP-Compliant equipment, software, ad study designs

BioReliance has significant experience (60+ years) managing studies within stringent regulatory guidelines

BioReliance® by SAFC

BioReliance

Toxicology Services

Bioanalysis and Toxicokinetic Report

Through the use of LC/MS/MS technology, BioReliance can analyze biological matrices from animal studies to produce a Toxicokinetics (TK) Report. Employing WinNonlin software available from PharSight, BioReliance will prepare a fully audited GLP report containing the parameters below:

T_{max}	Time for maximum drug concentration	(hour)
C_{max}	Maximum plasma concentration of drug	(ng/mL)
C_{min}	Minimum plasma concentration of drug	(ng/mL)
$AUC_{(0\text{-}inf)}$	Area under the plasma concentration-time curve (exposure)	
$T_{1/2}$	Elimination half-life	(hour)
MRT	Mean residence time	
Clearance	Volume of drug in blood cleared/unit time/unit body weight	(mL/hr/kg)

Available Services with Mass Spectrometry

		Standard		Toxicokinetics					
Area	**Assay**	Genetic Toxicology	Mammalian Toxicology	Genetic Toxicology	Mammalian Toxicology	**Assay Format**	**GXP****	**Test System**	**Assay Design**
Analytical Chemistry	Feasibility	✓	✓	✓	✓	LC/MS/MS	GLP	Biological Matrix	Evaluation of analytical method and extraction procedures
Analytical Method Validation	Transfer Validation	✓	✓	✓	✓	LC/MS/MS	GLP	Biological Matrix	Transfer Validation, sponsored-provided method
Analytical Method Validation	Full Validation	✓	✓	✓	✓	LC/MS/MS	GLP	Biological Matrix	Full Validation, BioReliance to develop method
Analytical Chemistry	Stability Analysis	✓	✓	✓	✓	LC/MS/MS	GLP	Biological Matrix or Vehicle Control	Analyze integrity of biological matrix
Analytical Chemistry	Metabolite Analysis			✓	✓	LC/MS/MS	GLP	Biological Matrix	Analyze metabolites in biological matrix
Analytical Chemistry	Dosing Matrix Analysis	✓	✓			LC/MS/MS	GLP	Biological Matrix or Vehicle Control	Measure propriety of biological matrix
Bioanalysis	Bioanalysis			✓	✓	LC/MS/MS	GLP	Biological Matrix	Analyze plasma samples from animal studies for TK parameters
Toxicokinetics	TK Analysis Report			✓	✓	WinNonlin software	GLP	Data	Report includes: PK/TK calculations with tables

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