Bioanalytical DMPK Services

BioAgilytix

BioAgilytix performs industry-standard DMPK assays for both small and large molecules. The drug metabolism research includes assessment of drug-drug interaction potential, metabolic stability, metabolite profile, and protein binding.

We will work with you to define the appropriate level of compliance based on the stage of your program, from the earliest discovery work all the way through post-market approval.

Drug Metabolism Assays

Metabolic Stability DMPK Assays

Metabolic stability DMPK assays are helpful when trying to determine the potential half-life of a compound when dosed to animals or humans. We determine the stability of a test article in a variety of enzyme sources, such as:

- Plasma
- Hepatocytes and other cultured cells
- Liver microsomal preparations
- Hepatic cytosol
- Hepatic S9 fraction
- Membrane preparations from recombinant bacteria or eukaryotic cells

Metabolite Profiling/ Characterization

We are able to generate and compare metabolite profiles to assist with species selection for toxicology studies. These studies are performed using accurate mass spectrometry (Exploris 240 Orbitrap) to analyze metabolic stability samples from liver microsome or hepatocyte incubations. *Ex vivo* plasma samples can also be searched for circulating metabolites.
By comparing profiles from toxicology studies and human clinical studies, we can identify unique or disproportionate human metabolites long before definitive radio labeled ADME studies to help avoid expensive delays.

Metabolites are characterized by:

- Exact mass
- Retention time
- Extracted ion chromatogram
- Fragmentation spectrum
- Isotope envelope

Drug-Drug Interaction Studies

We offer a range of *in vitro* services to evaluate the potential for drug-drug interaction, such as:

- CYP450 induction studies
- CYP/UGT inhibition studies
- CYP/UGT reaction phenotyping

Blood-To-Plasma Partition Ratio Determination

BioAgilytix performs blood-to-plasma partition ratio studies to determine the ratio of the distribution of test articles. Knowing the distribution of a drug candidate between red blood cells and plasma is useful for a number of reasons, including:

- Explaining variability in measured plasma concentrations due to hemolysis
- Over-predicted clearance values based on plasma concentrations when the compound actually distributes to the RBC compartment

Therefore, determining the blood-to-plasma ratio is important for deciding whether plasma or whole blood would provide more physiologically relevant pharmacokinetic parameters.

Protein Binding Assays

Equilibrium dialysis, ultrafiltration, or ultracentrifugation can be to determine the extent of drug binding to plasma or to proteins, such as:

- Human serum albumin
- α1-acid glycoprotein
- Gamma globulins
- Low density lipoprotein (LDL)
- High-density lipoprotein (HDL)
- Thyroxine binding globulin
- Prealbumin

Caco-2 Permeability Studies

The Caco-2 system is recognized as a predictive model that can help predict human intestinal absorption and oral bioavailability. By determining both the apical to basolateral (A-B) and the basolateral to apical (B-A) permeability, the efflux ratio can be calculated. Additionally, inhibition of the P-glycoprotein transporter can help determine if the test article is a P-gp substrate.

BioAgilytix

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