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ADME Services

CeeTox offers a full set of ADME services to advance your discovery and preclinical drug development activities.

We offer standard ADME services and advanced techniques and technologies to enable clients to make informed decisions that save money and dramatically improve the effectiveness of their drug discovery process. We:

- provide high quality data to support candidate advancement decisions
- enable our clients to identify unrealized potential in compounds classified as “problematic” in the discovery arena, so that opportunities are not missed
- help clients make better decisions on which candidates to actually terminate

We deliver knowledge, not just data

- High quality ADME profiling, data integration, predictive modeling
- Improved confidence in lead selection
- Experienced data interpretation with expert analysis

Specific ADME profiling includes:

- Solubility
- Permeability
- Transporter characterization
- Metabolic stability
- Metabolic inhibition
- Metabolite ID
- Protein affinity
- Partition coefficient (Log P/Log D)

The results – better candidates with greater frequency

- Improved predictability
- Reduced time to market
- Lower costs because of fewer later-stage failures



Leading the Field of *In Vitro* Toxicology



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President of PharMac LLC; Co-Chair of the Translational Module Advisory Panel for the NINDS, National Inst of Neurological Disorders and Stroke

ADME Analysis

We assist our customers with their ADME analysis, particularly with more problematic compounds or difficult assays that require more processing or analysis time. In addition to our higher levels of integrative modeling, we also perform industry-standard *in vitro* ADME profiling, including

- **Solubility** - HPLC/MS determination of solubility in aqueous buffers at pH 3 and 7 (including other pH values upon request) from DMSO stock; also including mixed aqueous systems such as simulated intestinal fluid, surfactants, and organic co-solvents. Quantitative evaluation of stability in aqueous buffers, simulated intestinal fluid is also available. Equilibrium studies from solid sample are available upon request.
- **Permeability** - Quantitative evaluation of bidirectional transport across Caco-2 and MDCK cell monolayers, analyzing both passive and active components; novel methods for assessing permeability of highly insoluble compounds.
- **Transporter Characterization** - Assessment of potential active transport and associated transporters, using Caco-2 monolayers and specific chemical inhibitors.
- **P-Glycoprotein DDI Potential** - Evaluation of Pgp substrate potential in MDR1-MDCK cells, compared to MDCK wildtype cells as controls. Inhibitor potential is determined by measuring decrease in Pgp transport of reference drugs, such as Digoxin or Quinidine, in the presence of test article, in MDR1-MDCK cells.
- **Metabolic Stability** - Qualitative evaluation of stability of a compound after incubation with mouse, rat, dog, monkey or human hepatic microsomes or hepatocytes, time course ($t_{1/2}$) and estimation of intrinsic clearance, examining both Phase I and Phase II mechanisms; other species and tissue microsomes available, as well as plasma stability. Optional identification of metabolites and qualitative species metabolite comparison.
- **CYP Inhibition** - Quantitative assessment of CYP inhibition (IC_{50}) by compounds of interest against known standards, in human liver microsomes.
- **Protein Binding** - Measured via equilibrium dialysis methods with mouse, rat, dog or human serum. Alternatively, ultrafiltration may be used.
- **Partition Coefficient (Log P/Log D)** - Octanol/water partitioning using LC/UV/MS detection for accurate concentration determinations in both phases over the log range of -3 to +3.

CeeTox continues to focus on the next generation of drug discovery challenges. We are developing new methods today to meet your emerging needs.