Hepatocyte Stability (mouse, rat)

Background: Drug metabolism and detoxification of about three quarters of all known drugs are primarily carried out in the liver. Hence, drug candidates have to be screened early in the discovery process for metabolic stability in order to rank them for further development and to predict in vivo hepatic clearance values. Hepatocytes contain the full range of both Phase I and Phase II drug metabolizing enzymes, hepatic transporters, and cofactors. Hepatocytes can, therefore, serve as a very good in vitro model to determine in vitro clearance of test compounds as well as their metabolites formation, likely to reflect the in vivo metabolic processes.

Service Details: Hepatocyte stability assay is performed using primary cryopreserved mouse or rat hepatocytes. Compounds at 3 μM concentration are incubated in presence or absence of hepatocytes at 37°C for 120 minutes. The reactions are performed in two replicates per compound and terminated with acetonitrile at each of the 6 sampling time points: 0, 5, 10, 30, 60 and 120 min incubation. The samples are then centrifuged and the relative parent compound depletion is determined by LC-MS/MS. The incubation of two positive control compounds with hepatocytes and a blank control reaction are used to verify assay validity.

Deliverable: Data include parent compound percent remaining. Full study report is provided.

Sample Submission: A minimal accurately weighable quantity of dry compound (~1 mg or 2 μmol) or 50 μL of 20 mM stock DMSO solution is required for this assay. For multiple ADME assays, lesser amount of compound per assay may be sufficient, depending on the particular project. We do not need to know structures of the molecules for ADME testing. However, brutto formulas have to be provided for all studies involving MS detection.