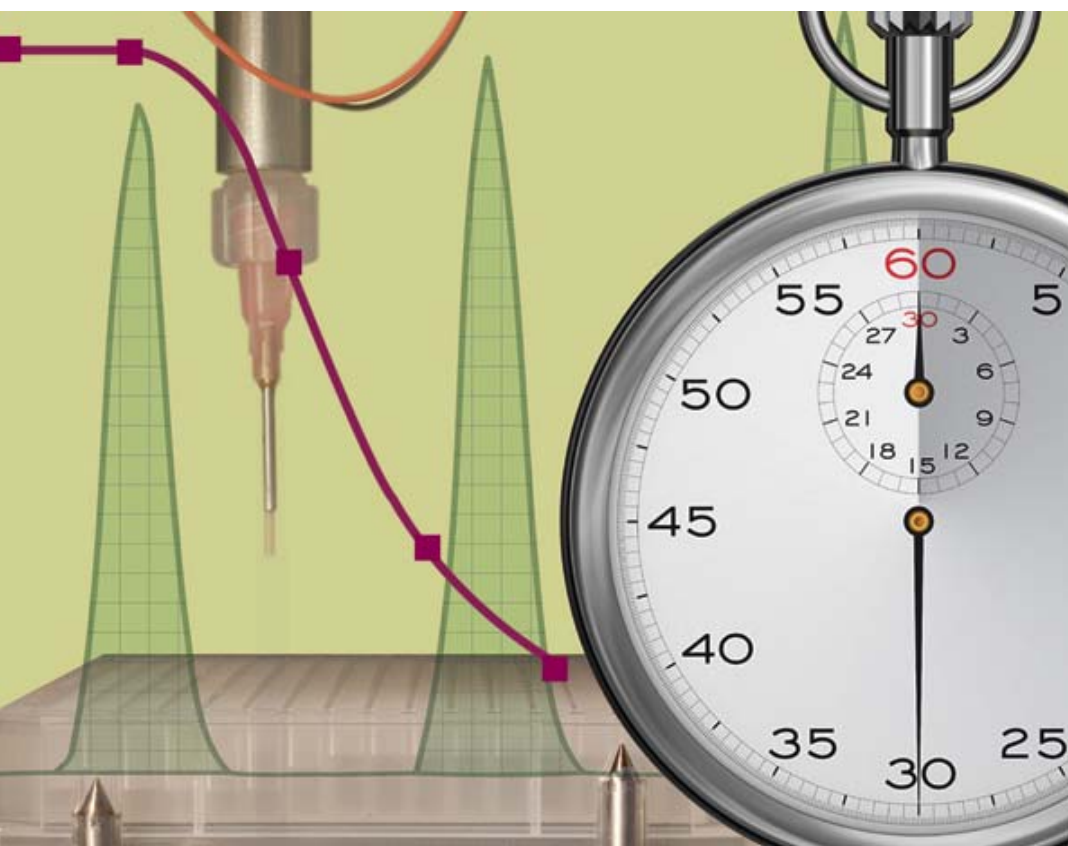


RapidFire® *In Vitro* ADME Applications



Faster ADME data – without compromises

Drug developers increasingly require faster and more predictive compound screens to reduce time-to-market and potential drug-drug interactions (DDI). With the BIOCIUS RapidFire® MS System, *in vitro* ADME assays can be performed using a reliable tool, the mass spectrometer, at unprecedented speeds without modifications to existing assay methods or workflow. With sample cycle times of approximately 6 seconds, the RapidFire system can obtain a 7 point IC50 curve in just 42 seconds – less time than a single sample analysis using standard HPLC-based methods. RapidFire data correlates very well with LC-MS analysis data for a spectrum of assays, i.e. CYP inhibition, metabolic stability and permeability, allowing researchers to utilize consistent assay analysis methods in drug discovery and drug development. The RapidFire system enables researchers to more efficiently utilize lab resources, obtain more data faster and make more informed decisions without compromising assay integrity.

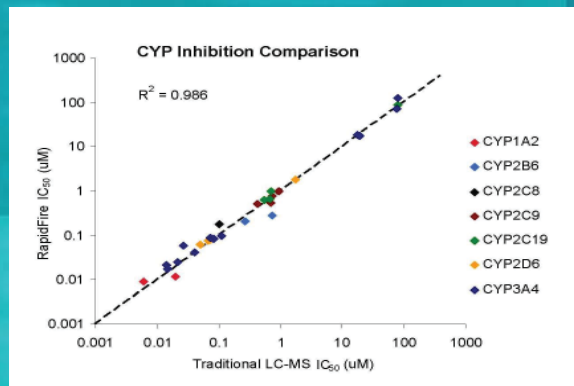
Applications

- CYP Inhibition
- Metabolic Stability
- Permeability
 - Caco-2 and PAMPA
- P-glycoprotein Inhibition
- CYP Induction
- Plasma Protein Binding

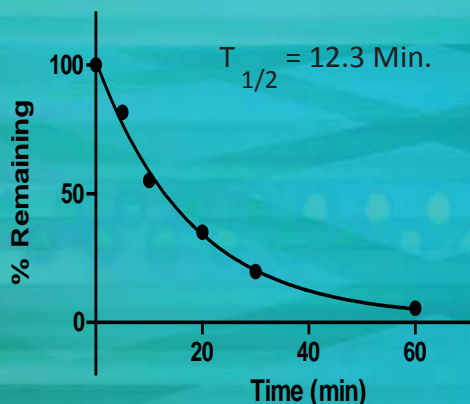
CYP Assays

CYP1A2	tacrine, melatonin
CYP2B6	bupropion
CYP2C8	amodiaquin, taxol
CYP2C9	tolbutamide, diclofenac
CYP2C19	S-mephenytoin, omeprazole
CYP2D6	dextromethorphan, bufuralol
CYP2E1	chlorzoxazone
CYP3A4/5	midazolam, testosterone, nifedipine, erythromycin

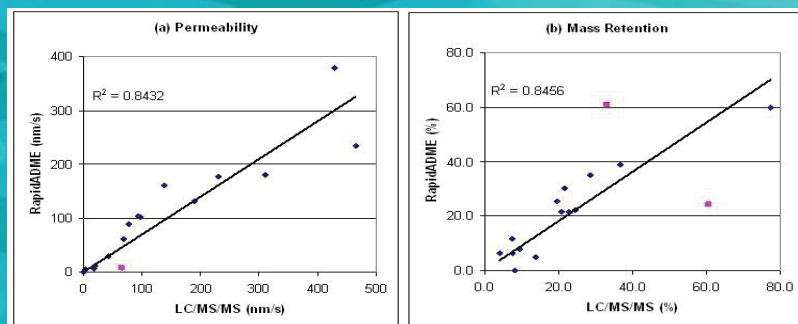
RapidFire can analyze FDA recommended drug probes



Correlation between traditional LC-MS and RapidFire: Data from 8 different enzyme/substrate pairs and 1 to 3 inhibitors for each pair conducted using traditional LC-MS at BD Biosciences and RapidFire technology at BIOCIUS. The dotted line represents a line of unity.



Example microsomal stability assay: Diclofenac (1 μM final concentration) was incubated with human liver microsomes (0.5 mg/ml). The reaction was initiated by the addition of NADPH and stopped by an acetonitrile + IS quench. Half-life was calculated based on first-order reaction kinetics.



Comparison of PAMPA results using RapidFire and LC-MS/MS: Sixteen compounds were tested: (a) Permeability, all but one (pink square) of these compounds were assigned the same permeability classes in both methods: low (<1.5), medium (1.5-20), or high (>20); (b) mass retention, 2 outliers (pink square) were not included in the regression analysis. (Data Courtesy of D.B. Kassel, Takeda San Diego, Inc. 2008)