Automation in Drug Discovery

Introduction

The use of automated sample processing, analytics and screening technology for profiling absorption, distribution, metabolism and excretion (ADME) early in the drug discovery process is becoming more widespread. State-of-the-art technology and automation allow for high-quality data to be generated rapidly and cost-effectively. To that end, WuXi DMPK has invested in several liquid handling station platforms to implement semi-automated assays. Semi-automation has the advantage of flexibility enabling manual intervention at the main stages of the assay for tasks that include loading reagents and transferring the samples to an incubator or centrifuge. WuXi DMPK has built a specialized automation team with more than 20 years of total experience in pharmaceutical automation applications. The team has worked seamlessly with clients from protocol discussion, automation validation to production.

Equipment

Hamilton MICROLAB STAR

The Hamilton MICROLAB STAR workstation is a midsize, flexible, automated robotic workstation that can be adapted to perform a variety of applications with a 96-channel pipetting head and 8 channels as well as a heating block and shaker. WuXi DMPK has successfully validated the plasma protein binding assay using a 96-well high-throughput dialysis (HTD) device. Data from 64 compounds using the Hamilton correlate very well with manual data as seen in Figure 2. The Hamilton has been validated for microsomal stability studies but hepatocyte stability study validation is ongoing.

Tecan FREEDOM EVO 150

The Tecan FREEDOM EVO 150 at WuXi is equipped with a 96-channel pipetting head. It is currently undergoing validation for routine biosample processing including serial dilutions and plasma protein precipitation. However, it has completed validation studies for 24-well MDCK permeability studies in Q4 2015.

Figure 2. Correlation of the measured percentage of unbound drug for 64 compounds in male Wistar Han rat plasma between manual data (abscissa) and Hamilton data (ordinate). Each data point represents the mean of 6 measurements.

Figure 3. Tecan FREEDOM EVO 150, an high-throughput workstation primarily used for permeability studies by WuXi DMPK.
Biomek FX 384

The Biomek FX at WuXi is equipped with a 384-channel pipetting head. This platform has supported the screening of over 40,000 compounds in metabolic clearance assays using liver microsomes and hepatocytes since 2009 and over 40,000 compounds screened for drug-drug interactions since 2012. The in vitro clearances of 10 commercial compounds were analyzed using the Biomek FX which correlated very well with data acquired manually as seen in Figure 5.

Figure 5. Correlation of the measured in vitro $t_{1/2}$ of 10 commercial compounds in human liver microsomes between manual data (abscissa) and Biomek data (ordinate). Each data point represents the mean of three separate runs.