



« P-gp Substrate Assessment services from Absorption Systems

» The CuBiAn, a fully-automated, bio-membrane-free chemical analyzer from Innovatis



## Channels of Discovery

### New tools for drug discovery

The drug discovery stage involves screening large numbers of compounds in a short period of time. The new, cutting-edge technology below can help you maximize your efforts in discovering the next important drug.

**Absorption Systems** announced that its **P-gp Substrate Assessment services** identify transporter-mediated drug-drug interactions for investigational new drugs (IND) in development. A recent FDA draft guidance recommends for sponsors of new drugs to fully explore how their drug interacts with other drugs. These data are sought by FDA not only for safety concerns, but to accelerate drug development programs as findings from early *in vitro* studies may serve to streamline later clinical investigations. Transporters are key in determining whether a drug gets into the body, how long it lasts, and whether two drugs will interact with positive or negative consequences. "By understanding transporters and the pathway a drug takes through the body, we better understand how to ensure that a compound doesn't overstay its welcome or cause unwanted side effects," says Patrick Dentinger, CEO of Absorption Systems, Exton, PA. "The ability to predict a clinical outcome from *in vitro* assays is exciting and understanding drug transporters is now officially part of the regulatory review process", adds Dentinger. P-gp, or P-glycoprotein, is a membrane transport protein that mediates the secretion of drug compounds by the intestine, liver and kidney, and also prevents such compounds from crossing the blood brain barrier. Compounds that are substrates or inhibitors of P-gp

can potentially participate in drug-drug or interactions. The Absorption Systems P-gp Substrate Assessment is an *in vitro* assay used to determine P-gp interaction with a test compound using MDRI-MDCKII cell monolayers in both the presence and absence of a P-gp inhibitor. As an *in vitro* assay, it may be performed at any stage in the drug development process. Therapeutics designed for chronic or subchronic administration are prime candidates for P-gp interaction assessment as they are most likely co-administered with other drugs. A minimum of 300µL of the test compound and its exact mass are required in order to perform the test. Bi-directional permeability data, efflux ratio in the presence and absence of the inhibitor and percent recovery of the test compound are provided. **More information: [www.absorption.com](http://www.absorption.com)**

**Innovatis** introduces **CuBiAn**, a fully-automated, bio-membrane-free chemical analyzer that measures key parameters in cell culture media, including **IgG**. As a proven, established technology, CuBiAn's automated capabilities and membrane-free technology allow for robust usage and high reproducibility, with very low operating costs in calibration and maintenance. All assays are prepared, incubated and measured by the instrument. Pipetting, barcode detection, sample dilution, temperature control are all automated. Unique to CuBiAn

technology, is its ability to detect IgG concentrations along with 11 different metabolites in a single sample and sequence. IgG is detected by immuno-turbidimetry, while all other molecules are quantified by photometric enzyme assays. This wide measurement range allows for a nearly unlimited flexibility for new assay methods. Capable of providing 90 results per hour (and 360 results with an ISE unit), CuBiAn requires a very low minimum sample volume, 2µL-35µL per test and less than or equal to 200µL minimum volume per sample. The key parameters measured are IgG (human, humanized), glucose, lactate, ammonia, glutamine, glutamate, inorganic phosphate, LDH, total protein, and Na<sup>+</sup>,K<sup>+</sup>,Cl<sup>-</sup>. **More information: [www.innovatis.com](http://www.innovatis.com)**

**Taconic** introduces the **HRN Mouse**, or the Hepatic Reductase Null Mouse, for improved studies in ADME-Tox facilitating drug efficacy screening, lead selection, and lead optimization. Originally developed by Cancer Research UK and commercialized by CXR Biosciences, this conditional, targeted knockout of Por (cytochrome P450 reductase) in the liver results in inactivation of all hepatic cytochrome P450 activity. As the cytochrome P450 system plays a major role in drug metabolism and disposition, this model is very useful for efficacy, bioavailability and ADMET studies. The lack of metabolism increases the circulating levels of compound



« The HRN mouse from Taconic

» The Thermo Scientific High-field Asymmetric waveform Ion Mobility Spectrometry (FAIMS)



thereby facilitating bioavailability studies and increasing the chances of demonstrating early *in vivo* efficacy. Although cytochrome P450 comprises a large, diverse family of proteins in both humans and animals, they can all be rendered inactive by deleting the gene for P450 reductase, the essential electron donor to all cytochrome P450 isozymes. After hepatic cytochrome P450 activity is eliminated, *in vivo* drug efficacy can be demonstrated more clearly and with much smaller amounts of valuable lead compounds. In addition, this model can also provide further information on whether parent compound or metabolite(s) are responsible for observed efficacy or toxicity when compared to wild-type mice. The lack of metabolism in the HRN also enables greater exposure to compounds without repeated dosing or the use of constant infusion pumps, even with high clearance compounds. The HRN mouse allows for the true dosing of parent compounds, which may not be otherwise possible. Because of the model's efficiency, researchers can look forward to reducing the number of experiments and animal use in lead selection, thus reducing costs. **More information: [www.taconic.com](http://www.taconic.com)**

**Thermo Fisher Scientific** announces innovative **Thermo Scientific High-field Asymmetric waveform Ion Mobility Spectrometry (FAIMS)** technology and its ability to remove interferences from a drug analysis. Using this method, researchers can adhere to the guidelines of the FDA to ensure human safety in drug development. Unforeseen analyte interferences can cause validated LC-MS methods to fail, resulting in costly delays in obtaining data from clinical trials. Another impact of co-eluting inter-

ferences is data misinterpretation, which could cause dosing errors in human test subjects. The FAIMS interface for the Thermo Scientific TSQ Quantum series of mass spectrometers works in combination with the H-ESI and APCI ion probes at atmospheric pressure to increase selectivity during analysis. FAIMS provides additional ion filtering, resulting in LC-MS/MS chromatograms with reduced chemical background and endogenous interferences. **More information: [www.thermo.com](http://www.thermo.com)**

**Advanced Chemistry Development (ACD/Labs)** announces the release of its latest version of **ACD/Labs PhysChem software**. Version 11 provides updated molecular property predictions for a broader variety of chemical classes through enhanced models; and offers a new customizable interface for instant interactive review of results. One of the updates is a new  $\log P$  prediction model based on experimental data from more than 25,000 compounds. Substantial increase of the internal database (the training set) from version 10, with experimental data, has expanded and diversified chemical space coverage, particularly for compounds of pharmaceutical interest. Enhancements to ACD/ $pK_a$  DB come from the addition of over 2,500 new compounds and experimental data into the training database, resulting in increased chemical space coverage and greater prediction accuracy. Since the PhysChem product line is heavily integrated, improvements to the  $\log P$  and  $pK_a$  models augment the prediction quality of our whole range of predictive software products. Their most popular applications that predict pH profiles of the distribution coefficient ( $\log D$ )

and aqueous solubility use  $\log P$  and  $pK_a$  predictions in the background and will therefore be influenced by the new and enhanced models. To further accommodate novel or proprietary chemistry, version 11 brings improvements to our algorithm training capabilities to encourage more frequent use of in-house experimental data for improving prediction accuracy. This will help computational chemists ensure that quality predictive models are available for the proprietary chemical classes their researchers might be exploring in the future. **More information: [www.acdlabs.com](http://www.acdlabs.com)** ■

Companies Mentioned in this Product Spotlight:

Absorption Systems - [www.absorption.com](http://www.absorption.com)

ACD/Labs - [www.acdlabs.com](http://www.acdlabs.com)

Innovatis - [www.innovatis.com](http://www.innovatis.com)

Taconic - [www.taconic.com](http://www.taconic.com)

Thermo Scientific - [www.thermo.com](http://www.thermo.com)

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