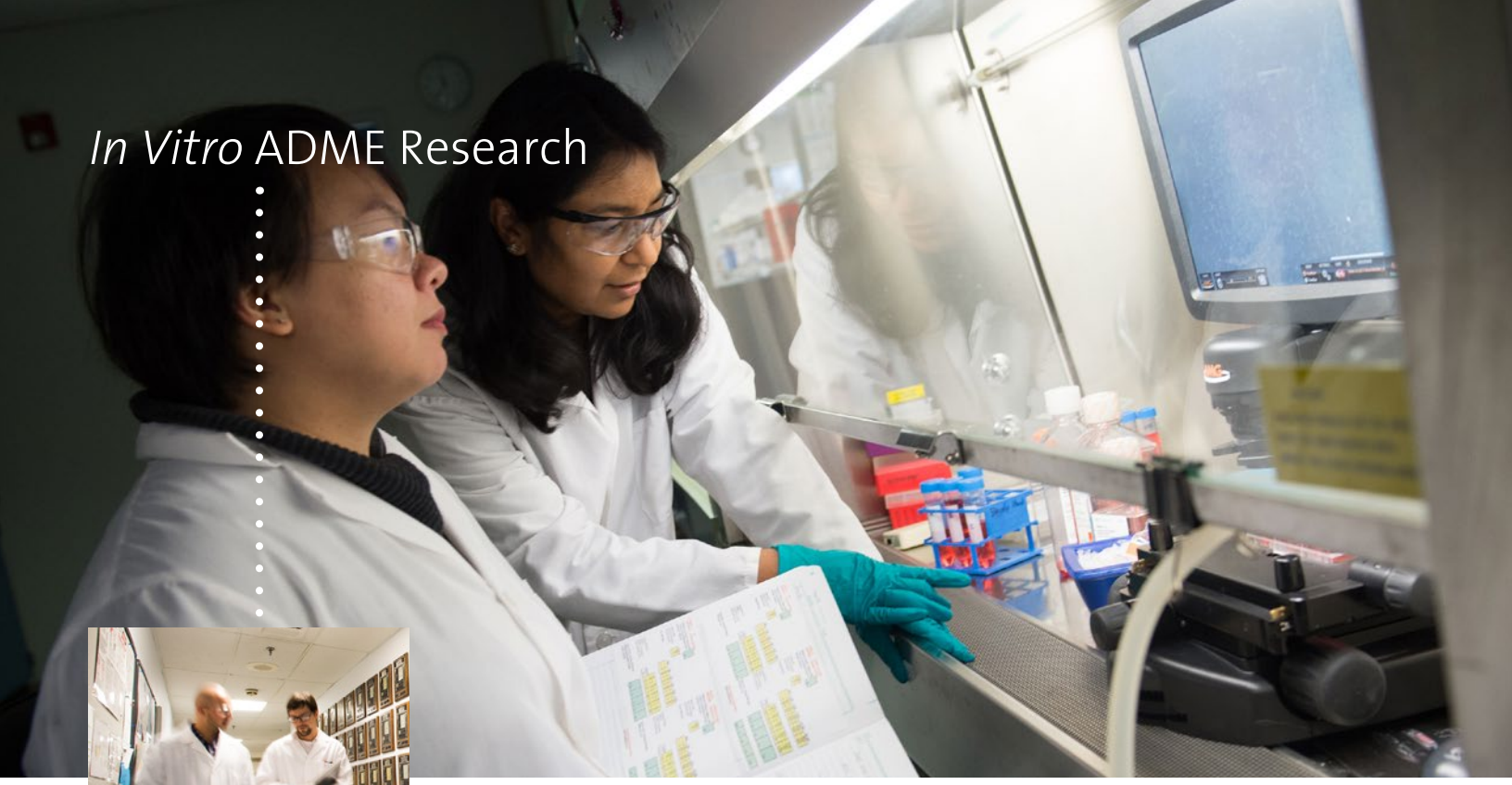
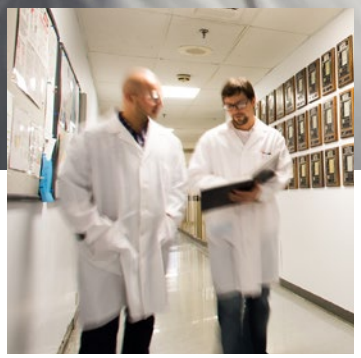
Corning® Gentest™ Contract Research Services

Integrated Contract Services to support *in vitro* analysis of xenobiotic absorption, transport, and metabolism

CORNING

In Vitro ADME Research





Support you can count on

Corning ADME services has a long history of successful customer audits and a 100% acceptance of data by regulatory agencies.

Personalized guidance to help you make decisions quickly and efficiently

Successful drug development projects require making choices that can dramatically affect the success of your business well into the future. With the proper information, you can become more efficient and more assured you are proceeding on a viable path to FDA approval.

Corning® Gentest℠ Contract Research Services combines industry leading proprietary products, advanced technology, and personalized guidance from expert study directors to deliver reliable, submission-ready results.

When you work with Corning, you have access to:

Experience

For more than 20 years, our Contract Research Services team has been developing and conducting *in vitro* drug-drug interaction studies to support hundreds of pharmaceutical discovery and development projects.

Skilled, Attentive Study Directors

Our scientists are experts in the areas of drug absorption, transport, metabolism, induction, toxicity, and regulatory guidance. We'll stay in close communication with you throughout your study to facilitate informed decisions.

Regulatory Guidance Alignment

Study designs are continually updated to align with current Regulatory Agency guidance—so you can be assured you'll have the right data for submission to the FDA, EMA, or MLHW.

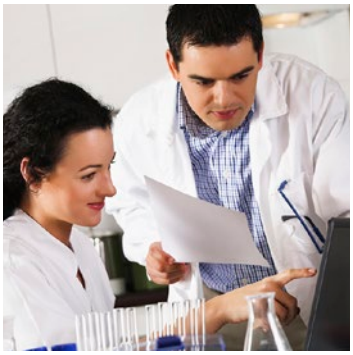
Quality Data and Reports

You can depend on our team for accurate, reproducible data, and high-quality, well-written reports. Whether your study is conducted GLP or nonGLP, you will receive a data package you can count on.

Custom Assay Services

Corning has expertise in adapting clients' protocols to facilitate comparison with existing client databases. Customizations may include the choice of extracellular matrix, treatment media, positive control-inducing chemical/concentration, as well as many other client-specified adaptations. In addition, we can fulfill many other study requests in line with our core competencies of enzymology, analytical chemistry, and cell-based assays.

The ADME services you need to make important drug development decisions



Corning® Gentest℠ Contract Research Services Portfolio

Our team of experts can design studies to predict drug-drug interactions and human pharmacokinetics using the innovative Corning Gentest™ *in vitro* products, cell models, and methodologies. Services include:

Transporter Interaction Studies

- SLC transporter studies with Corning TransportoCells™ study models
- P-gp/MRP/BCRP/BSEP membranes and vesicles studies
- Efflux studies with MDR1 LLC-PK1 and Caco-2 cell lines

Enzyme Induction

- *In vitro* models in human hepatocytes that enable predicting enzyme induction *in vivo*
- Multiple endpoints including EC_{50}, E_{max}, and RIS
- Comprehensive portfolio of inducible enzymes, including CYPs 1A2, 2B6, 2C8, 2C9, 2C19, 3A4, UGTs, and transporters
- Research methods aligned with regulatory guidance
- Testing options for both definitive evaluation, higher throughput, and lead optimization

Enzyme Inhibition

- Reversible and time-dependent enzyme inhibition studies
- Major and minor CYPs, UGTs, and other enzymes
- IC_{50} values, K_i, K_I, k_{inact}; experimental designs aligned with regulatory guidance
- Microsomes and/or hepatocytes as enzyme sources
- Fully validated LC/MS/MS methods

Reaction Phenotyping

- Enzyme identification using Corning Supersomes™ enzymes, chemicals, antibodies, pooled and single-donor human liver microsomes
- Over 40 cDNA-expressed drug metabolizing enzymes available for the most comprehensive evaluation

Metabolic Stability in Microsomes and/or Hepatocytes

- Assays to predict the intrinsic clearance or metabolic half-life of a test article
- Performed in human and pre-clinical animal liver microsomes or Hepatocytes

Permeability and Transport

- Permeability testing, P-gp transport, and inhibition screening using Caco-2 and MDR1-LLC-PK1 monolayers

Plasma Protein Binding

- High throughput, cost-effective equilibrium dialysis method

Custom Designed Studies

- Unusual drug metabolizing enzymes, custom expressions, extrahepatic tissues, assay transfers

Contact us via email at ADMETOX@corning.com, or call 781.938.2546.

A leading provider of *in vitro* ADME Contract Research Services for over 20 years

Founded by Dr. Charles Crespi, a pioneer and influential contributor in the field of ADME/Tox studies, Corning Gentest contract services brings together decades of experience in the pharmaceutical drug discovery and development programs in early and late ADME/Tox phase.

Recent Publications by Corning® Gentest℠ Contract Research Service Staff

1. Zhang J-G, Ho T, Callendrello AL, Clark RJ, Santone EA, Kinsman S, Xia D, Fox LG, Einolf HJ, and Stresser DM (2014), Evaluation of Calibration Curve-based Approaches to Predict Clinical Inducers and Non-inducers of CYP3A4 with Plated Human Hepatocytes. Drug Metab Dispos, 42:1379-91.
2. Stresser DM, Mao J, Kenny JR, Jones BC, Grime K (2014), Exploring Concepts of In Vitro Time-dependent CYP Inhibition Assays. Exp Op Drug Metab Toxicol. 10:157-174.
3. Ellens H, Deng S, Coleman J, Bentz J, Taub ME, Ragueneau-Majlessi I, Chung SP, Herédi-Szabó K, Neuhoff S, Palm J, Balimane P, Zhang L, Jamei M, Hanna I, O'Connor M, Bednarczyk D, Forsgard M, Chu X, Funk C, Guo A, Hillgren KM, Li L, Pak AY, Perloff ES, Rajaraman G, Salphati L, Taur JS, Weitz D, Wortelboer HM, Xia CQ, Xiao G, Yamagata T, Lee CA (2013), Application of Receiver Operating Characteristic Analysis to Refine the Prediction of Potential Digoxin Drug Interactions. Drug Metab Dispos. 41:1367-1374.
4. Bentz J, O'Connor MP, Bednarczyk D, Coleman J, Lee C, Palm J, Pak YA, Perloff ES, Reyner E, Balimane P, Brännström M, Chu X, Funk C, Guo A, Hanna I, Herédi-Szabó K, Hillgren K, Li L, Hollnack-Pusch E, Jamei M, Lin X, Mason AK, Neuhoff S, Patel A, Podila L, Plise E, Rajaraman G, Salphati L, Sands E, Taub ME, Taur JS, Weitz D, Wortelboer HM, Xia CQ, Xiao G, Yabut J, Yamagata T, Zhang L, Ellens H. (2013), Variability in P-glycoprotein Inhibitory Potency (IC_{50}) Using Various In Vitro Experimental Systems: Implications for Universal Digoxin Drug-Drug Interaction Risk Assessment Decision Criteria. Drug Metab Dispos. 41:1347-13466.
5. Zhang J-G and Stresser DM (2013), "Evaluation of Time-Dependent Inhibition of CYP3A4 in Human Hepatocytes" in "Optimization in Drug Discovery: In Vitro Methods" (Z Yan and GW Caldwell eds) in series "Methods in Pharmacology and Toxicology (YJ Kang, series ed), Humana Press, Totowa, NJ, USA.
6. Stresser DM and Zhang J-G (2013), "Higher-throughput Screening Methods to Identify Cytochrome P450 Inhibitors and Inducers: Current Applications and Practice" in High Throughput Screening Methods in Toxicity Testing, Wiley Press. Pablo Steinberg, Ed.
7. Henne KR, Thuy BT, VandenBrink BM, Rock DA, Aidasani D, Subramanian R, Mason AK, Stresser DM, Teffera Y, Wong SG, Johnson MG, Chen X, Tonn GR, and Wong BK (2012), Sequential Metabolism of AMG 487, a Novel CXCR3 Antagonist, Results in Formation of Quinone Reactive Metabolites that Covalently Modify CYP3A4 Cys239 and Cause Time-dependent Inhibition of the Enzyme. Drug Metab Dispos. 40:1429-1440.
8. Elsby R, Smith V, Fox L, Stresser D, Butters C, Sharma P, Surry DD (2011), Validation of Membrane Vesicle-based BCRP and MRP2 Assays to Assess Drug Transport and the Potential for Drug-Drug Interaction to Support Regulatory Submissions. Xenobiotica, 41:764-783.
9. Elsby R, Fox L, Stresser DM, Layton M, Butters C, Sharma P, Smith V, Surry DD (2011), In Vitro Risk Assessment of AZD9056 Perpetrating a Transporter-mediated Drug-Drug Interaction with Methotrexate. Eur J Pharm Sci 43:41-49.
10. Zhang J-G, Ho T, Callendrello AL, Crespi CL, Stresser DM (2010), A Multi-endpoint Evaluation of Cytochrome P450 1A2, 2B6, and 3A4 Induction Response in Human Hepatocyte Cultures after Treatment with beta-Naphthoflavone, Phenobarbital, and Rifampicin. Drug Metab Lett. 4:185-194.
11. McGinnity DF, Zhang J-G, Kenny JR, Hamilton GA, Otmani S, Stams KR, Haney S, Brassil P, Stresser DM, and Riley RJ (2009), Evaluation of Multiple In Vitro Systems for Assessment of CYP3A4 Induction in Drug Discovery: Human Hepatocytes, Pregnane X Receptor Reporter Gene, and Fa2N-4 and HepaRG Cells. Drug Metab Dispos. 37:1259-1268.
12. Perloff ES, Mason AK, Dehal SS, Blanchard AP, Morgan L, Ho T, Dandeneau A, Crocker RM, Chandler CM, Boily N, Crespi CL, and Stresser DM (2009), Validation of a Cytochrome P450 Time-dependent Inhibition Assay: A Two Time Point IC50 Shift Approach Facilitates Kinact Assay Design. Xenobiotica 39:99-112.
13. Stresser DM, Mason AK, Perloff ES, Ho T, Crespi CL, Dandeneau AA, Morgan L and Dehal SS (2009), Differential Time- and NADPH-dependent inhibition of CYP2C19 by Enantiomers of Fluoxetine. Drug Metab. Dispos. 37:695-698.

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