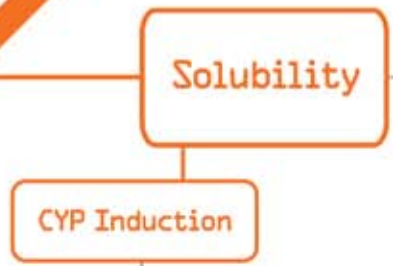
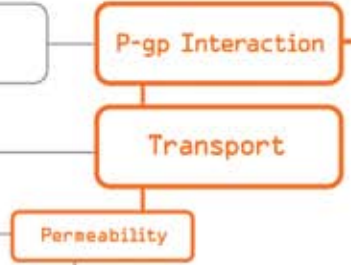
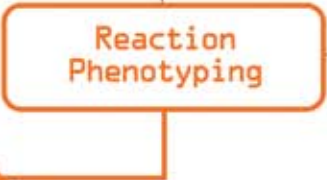


IN VITRO ADME DISCOVERY SCREENING RESEARCH SERVICES

The most rapid path to more **sound decision making.**



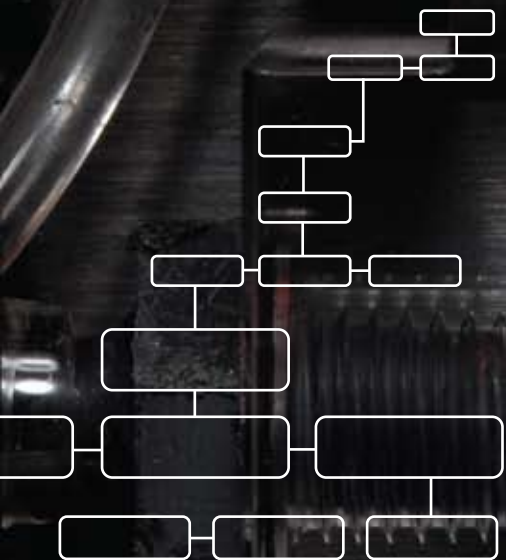
Helping all people live healthy lives



The information you need to make important drug discovery decisions.

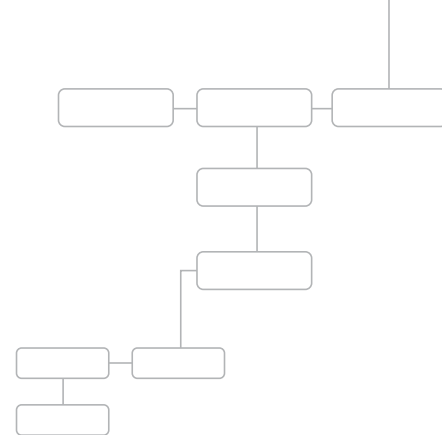
Drug discovery screening requires making choices that can dramatically affect the success of your business well into the future. With the proper information, you can become more efficient and more assured you are proceeding on a viable path in pursuit of the next treatment or cure. That is why BD Biosciences ADME Contract Research Services delivers a unique combination of industry leading proprietary products, advanced technology, personalized guidance from expert study directors and reliable, submission-ready results. Together, these elements provide you with the most rapid path to more sound decision making in your drug discovery endeavors. Choose BD and move forward with confidence.

To inquire about BD Biosciences ADME Contract Research Services, please see contact details on the back of this brochure, or visit bdbiosciences.com/offices to locate your nearest BD Biosciences office.





THE MOST rapid path to more sound decision making.



TESTED SCIENCE. RELIABLE RESULTS.

Drug developers now require faster and more predictive compound screens to reduce time-to-market and potential drug-drug interactions. BD Biosciences ADME Contract Research Services group works as an extension of a client's team to provide reliable data and faster results. Utilizing state-of-the-art techniques, products, and equipment, BD Biosciences is able to assist clients in screening for viable drug candidates during drug discovery or by preparing regulatory agency submission-quality reports for your drug development compounds.

Only BD Biosciences Contract Research Services delivers a combination of industry leading proprietary products, advanced technology, expert guidance from renowned study directors and reliable, submission ready results. Together, these elements provide you with the most rapid path to more sound decision making in your drug discovery endeavors.

Expert Study Directors that facilitate informed decisions.

BD Biosciences ADME Contract Research Study Directors have been helping customers test their drug compounds for over 15 years. Our Study Directors are highly skilled scientists with in-depth knowledge of absorption, transport and metabolism. This expertise gives BD Biosciences Study Directors the ability to partner with clients to develop and deliver a broad range of in vitro ADME studies to meet their discovery and development project needs. BD ensures the highest level of quality standards and adheres to current regulatory requirements and applicable FDA-sponsored guidance documents.

Advanced technology and leading processes.

BD Biosciences uses leading-edge technology, like RapidFire® high-throughput mass spectroscopy for CYP Inhibition and the unique BD solubility scanner for solubility testing. Our industry leading brand of products including BD Supersomes™, BD Gentest™ hepatocytes, human liver microsomes, transporter proteins, BD BioCoat™ assay systems, and BD Falcon™ inserts, make BD Biosciences the company clients have come to rely on and trust. The combination of advanced technology, processes and latest product offering, including use of BD's new BD UltraPool™ HLM 150 donor pool, combine to deliver high quality, accurate and rapid results. Through every step of the drug discovery process, sponsors will work directly with our highly specialized Study Directors who will respond efficiently to the rapidly changing technology.

BD BIOSCIENCES ADME DISCOVERY SERVICES

- 03 Enzyme Inhibition Studies
- 05 Permeability and Transport Studies
- 06 High-throughput Reaction Phenotyping
- 07 Metabolic Stability Studies
- 09 Protein Binding Studies
- 11 Solubility and Aggregation Studies

CYP INHIBITION expertise



HIGH-THROUGHPUT CYP INHIBITION SERVICE WITH FDA-RECOMMENDED PROBE SUBSTRATES.

Inhibition of cytochrome P450 enzyme catalytic activity is a leading mechanism of metabolism-based drug-drug interactions. In vitro inhibition studies are valuable predictors of in vivo drug-drug interactions and the magnitude of that interaction. In many cases, this information can eliminate the need for further in vivo studies. The in vitro ADME market leader in P450 products and services, BD Biosciences, and the technology leader in high-throughput mass spectrometry, BIOCIUS Life Sciences, Inc., are combining expertise to provide a novel mass spectrometry-based, high-throughput complete service package for cytochrome P450 inhibition. BD Biosciences CYP Inhibition Services deliver high-quality data analysis with use of BD UltraPool™ HLM 150 liver microsomes. Complete package of sample preparation and rapid turnaround of data analysis is provided at the conclusion of this service.

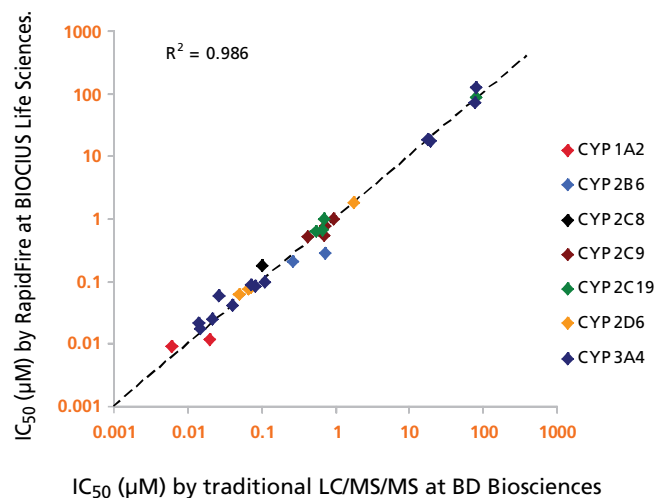


Elke S. Perloff

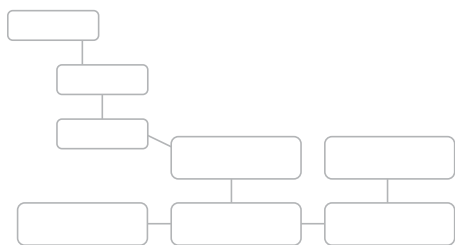
STUDY DIRECTOR

Dr. Elke S. Perloff has been a Study Director with BD Biosciences for over 5 years, contributing her expertise in the areas of drug transport and P450 mediated metabolism. Elke serves as a Study Director for transport, permeability, P450 inhibition, metabolic stability, reaction phenotyping, and protein binding projects in addition to responsibilities as Head of Operations. Elke received her Ph.D. in Pharmaceutical Sciences from Humboldt University, Berlin, Germany, including working as a postdoctoral fellow in Clinical Pharmacology and completed research in the areas of P450 metabolism and P-gp transport, inhibition and induction at Tufts University in Boston, MA. Dr. Elke Stormer Perloff has published over 25 articles in peer-reviewed scientific literature in the areas of in vitro drug metabolism, drug transport, and drug interactions.

CORRELATION DATA BETWEEN CONVENTIONAL LC/MS AT BD BIOSCIENCES AND RAPIDFIRE® AT BIOCIUS LIFE SCIENCES, INC.



Data from 8 different enzyme/substrate pairs and 1 to 3 inhibitors for each pair was generated using traditional LC/MS/MS at BD Biosciences and RapidFire® technology at BIOCIUS Life Sciences, Inc. Inhibitors include ketoconazole, alpha-naphthoflavone, montelukast, S-benzylirvanol, sulfaphenazole, azamulin, paroxetine, ticlopidine, S-fluoxetine, tienilic acid, verapamil, and diltiazem.



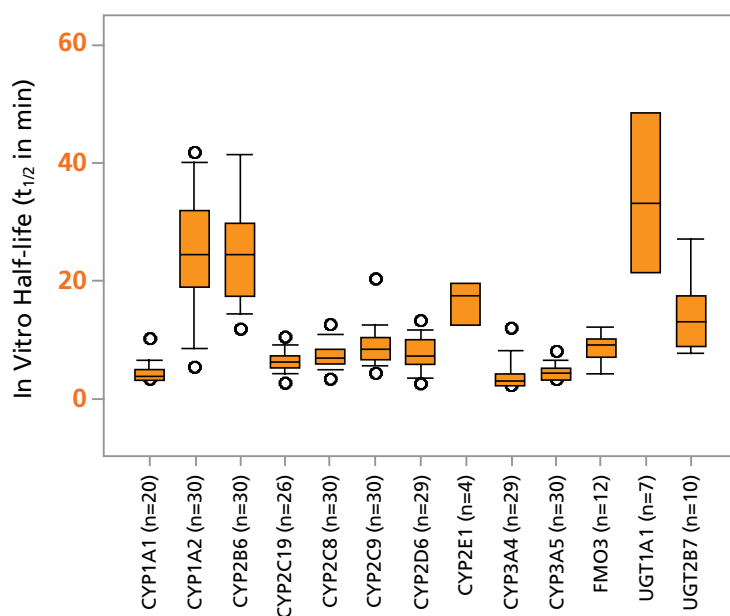
REACTION PHENOTYPING expertise

ENZYME IDENTIFICATION BY SUBSTRATE LOSS ANALYSIS USING BD SUPERSOMES™ ENZYMES.

Reaction phenotyping studies help identify the number and identity of P450, UGT or other enzyme-mediated pathways of elimination – important information that affects population variability in metabolism and the risk of becoming a victim drug in a drug-drug interaction event. Using BD Supersomes™, the gold standard for recombinant metabolizing enzymes, is a key element to delivering reproducible results. Enzyme concentrations for specific enzymes are fixed or scaled to provide activity proportionate to the average content in human liver microsomes. Enzyme content can be optimized for higher turnover– important for low-clearance drug candidates.



HISTORICAL ASSAY PERFORMANCE FOR HIGH-THROUGHPUT REACTION PHENOTYPING USING BD SUPERSOMES ENZYMES



| Enzyme | Probe Substrate | Enzyme conc. | Substrate conc. |
|---------|------------------|--------------|-----------------|
| CYP1A1 | Amodiaquine | 100 pmol/mL | 10 μM |
| CYP1A2 | Phenacetin | 100 pmol/mL | 10 μM |
| CYP2B6 | Bupropion | 50 pmol/mL | 1.0 μM |
| CYP2C19 | Omeprazole | 100 pmol/mL | 10 μM |
| CYP2C8 | Amodiaquine | 25 pmol/mL | 10 μM |
| CYP2C9 | Diclofenac | 25 pmol/mL | 10 μM |
| CYP2D6 | Dextromethorphan | 50 pmol/mL | 10 μM |
| CYP2E1 | P-nitrophenol | 100 pmol/mL | 1.0 μM |
| CYP3A4 | Midazolam | 25 pmol/mL | 5.0 μM |
| CYP3A5 | Midazolam | 25 pmol/mL | 5.0 μM |
| FMO3 | Benzylamine | 0.5 mg/mL | 0.1 μM |
| UGT1A1 | Estradiol | 0.5 mg/mL | 2.5 μM |
| UGT2B7 | 7-HFC | 0.5 mg/mL | 5.0 μM |

In vitro half-life results obtained for positive controls under the conditions listed in the table. Boxes represent the 25th-75th percentile, the line indicates the median, error bars indicate the 90th and 10th percentiles, and circles represent outliers outside the 5th/95th percentiles. Data was obtained using multiple lots of BD Supersomes enzymes on independent days.

PERMEABILITY AND TRANSPORT expertise



P-GP INTERACTION ASSESSMENT WITH CACO-2 OR MDR1-LLC-PK₁ CELL MONOLAYERS.

Bidirectional transport assays across Caco-2 and MDR1-LLC-PK₁ monolayers comply with the FDA recommended approach to determine apparent permeability of a test article and assess P-glycoprotein (P-gp) mediated transport and inhibition. Only BD Biosciences Contract Research Services delivers a combination of industry leading proprietary products, advanced technology, expert guidance from renowned Study Directors and reliable, submission ready results. Together, these elements provide you with the most rapid path to more sound decision making in your drug discovery endeavors.

Caco-2 is the in vitro gold standard method to evaluate test article permeability (P_{app})

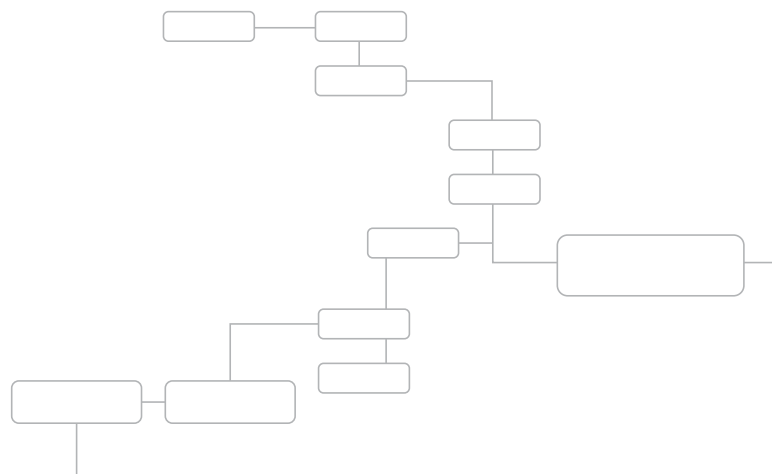
An important factor in oral bioavailability is the ability of a compound to be well absorbed in the small intestine. Polarized cell monolayers have become the gold standard in in vitro test systems to quickly and cost effectively assess the permeability of a test article. Caco-2 cells resemble small intestinal epithelial cells in morphology and expression of certain enzymes and transporters. It is the most frequently used cell line for permeability testing and the recommended approach to rank order compounds according to the FDA's Biopharmaceutics Classification System (BCS) as low, medium, or high permeability compounds^[1].

Caco-2 and MDR1-LLC-PK₁ cell lines are well characterized for efflux transporter activity

Efflux transporters other than P-gp, such as breast cancer resistance protein (BCRP) and multidrug resistance-associated protein (MRP2) can be expressed in commonly used cell lines such as MDCK. BD's Caco-2 and MDR1-LLC-PK₁ cells are characterized for P-gp, BCRP, and MRP2 activity facilitating interpretation of efflux results.

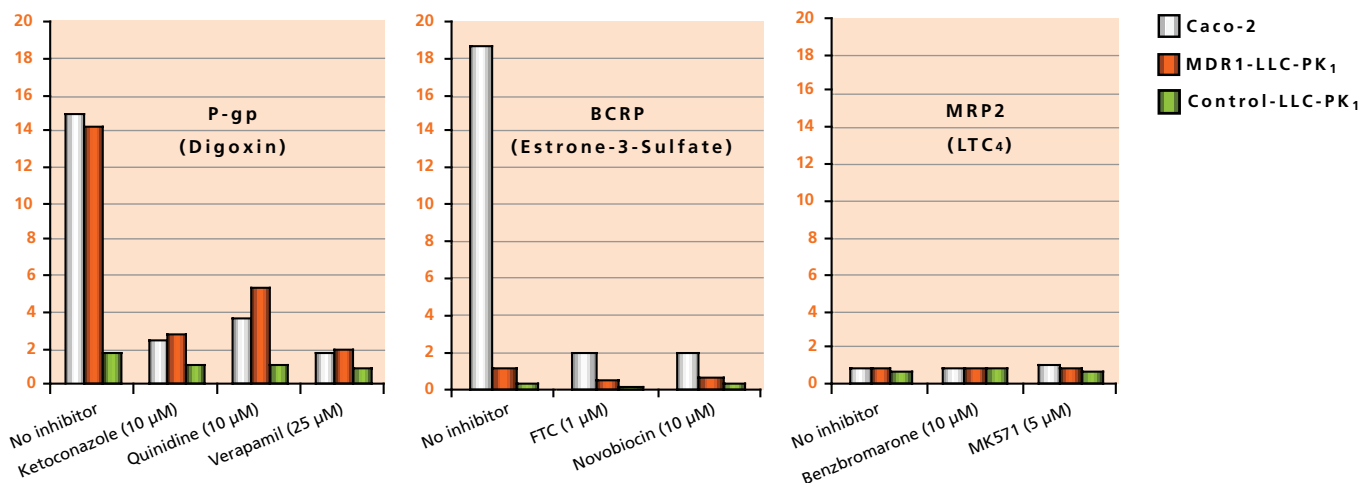
FDA recommends bidirectional transport assays in polarized cell models to identify substrates and inhibitors of P-glycoprotein

Transporter proteins expressed in various tissues including intestinal epithelium, kidney, liver, and blood-brain barrier are recognized for their effects on drug disposition. Current-FDA guidance^[2] recommends the testing of investigational drugs for interactions with P-glycoprotein (P-gp) using bidirectional transport assays in polarized cell models. Caco-2 and MDR1-LLC-PK₁ cells both show high levels of P-gp activity making them excellent models for P-gp-mediated drug transport studies.



[1] U.S. FDA/CDER, Biopharmaceutics Classification System (BCS), August 2000.
[2] U.S. FDA/CDER, Drug Interaction Studies - Study Design, Data Analysis, and Implications for Dosing and Labeling, DRAFT GUIDANCE, September 2006.

EFFLUX TRANSPORTER ACTIVITY IN CACO-2 AND LLC-PK₁ CELL MONOLAYERS



P-gp, BCRP, and MRP2 transporter activity assessment in Caco-2 and LLC-PK₁ cell monolayers. Data represents efflux ratios of each probe substrate and the effects of prototypical inhibitors on the activity of each transporter. Efflux ratios were generated from mean A-B and B-A P_{app} values of duplicate monolayers.

Efflux of the P-gp probe substrate digoxin was observed in both Caco-2 and MDR1-LLC-PK₁ cells, and can be inhibited by the known P-gp inhibitors ketoconazole, quinidine, and verapamil. Efflux of the BCRP probe substrate estrone-3-sulfate (E3S) was observed in Caco-2 cells only, with an efflux ratio similar to that of digoxin. E3S efflux is significantly inhibited by the BCRP inhibitors novobiocin and fumitremorgin C (FTC). No efflux was observed for the MRP2 substrate LTC₄ in either Caco-2 or MDR1-LLC-PK₁ cells. LLC-PK₁ control cells showed no efflux activity for any of the probe substrates.

EXPRESSION OF HUMAN MDR1 cDNA CELL LINES.

MDR1-LLC-PK₁ and Caco-2 cell monolayers are widely used for permeability and transporter interaction studies for assessment of P-glycoprotein (P-gp)-mediated drug transporter interactions as recommended by the USFDA.

MDR1-LLC-PK₁ cells predominantly express human P-gp against a low background of porcine P-gp and other transporters making MDR1-LLC-PK₁ an excellent model to study human P-gp specifically. This is unlike Caco-2 cells that exhibit both human P-gp and BCRP (Kapadnis et al, 2009 Drug Met Rev. Abstr. no 359). BD Biosciences holds the exclusive rights for the expression of human MDR1 cDNA cell lines for use in research products and services.



Lisa Fox
STUDY DIRECTOR

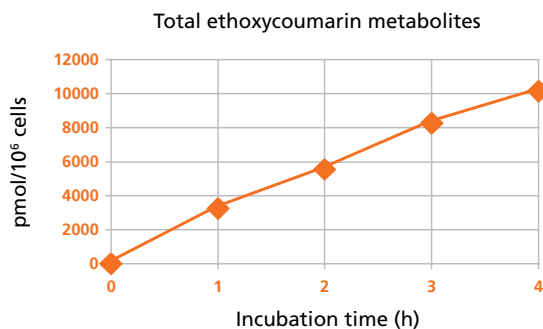
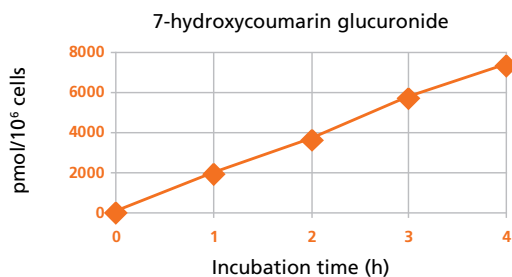
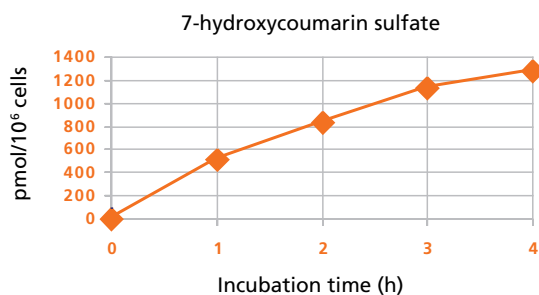
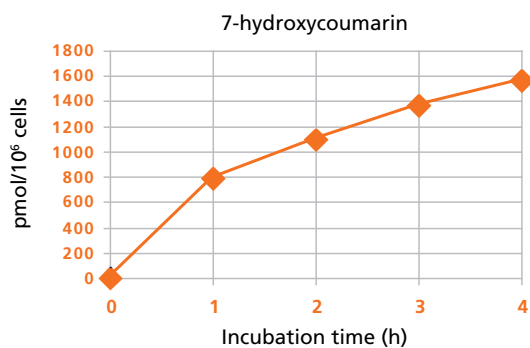
Lisa is a Senior Research Scientist and Study Director working in the area of ADME cell-based products and services. In her eleven years at BD Biosciences, Lisa's main R&D focus has been in the development of transporter models and services (hepatocytes, Caco-2 and transporter cDNA-expressing cell lines, membranes vesicles, oocytes, and cell culture insert systems). In her role as a Study Director within the ADME Contract Research Services group, Lisa directs drug-transporter interaction, permeability, and plasma protein binding studies in both Discovery and Development platforms. Before joining BD Biosciences, Lisa worked in the Clinical Pharmacokinetics and Disposition department of a large pharmaceutical company, and in a Harvard/BIDMC research group studying the roles and functions of mast cells.

METABOLIC STABILITY expertise



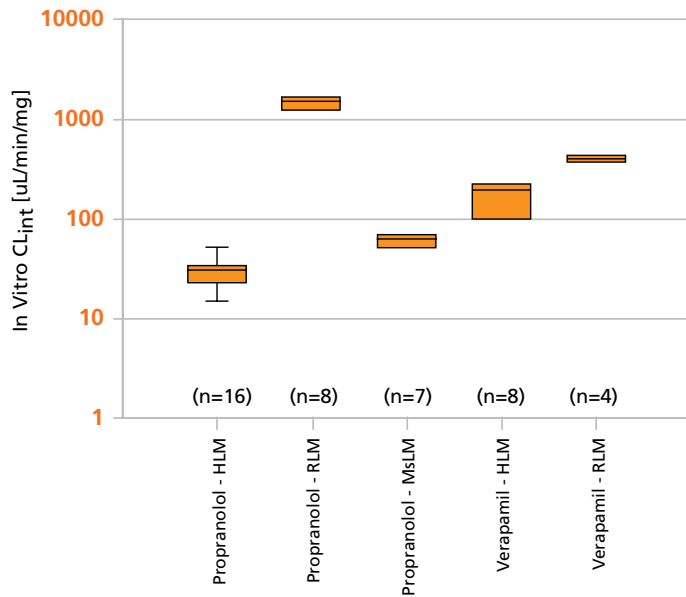
Metabolic stability assays measure the stability of a test compound by incubating the test compound with liver microsomes, hepatocytes, or S9 enzyme sources from human and animal species. Evaluating primary metabolism and pharmacokinetics in the liver helps identify whether a compound is chemically stable and metabolized at an acceptable rate within the body. BD Biosciences provides rapid in vitro metabolic stability testing using several different enzyme sources. Most often, this test utilizes hepatocytes or liver microsomes. BD Biosciences metabolic stability testing using hepatocytes features a carefully selected, single freeze, mixed gender 10-human donor pool and results provided for human and preclinical species. Our metabolic stability testing using microsomes maintains data consistency from assay-to-assay with mixed gender human liver microsomes donor pool consisting of 150 donors. Results are highly reproducible over extended periods of time using various lots of microsomes.

TIME COURSE OF ETHOXYCOUMARIN METABOLISM IN HUMAN CRYOPRESERVED HEPATOCYTES



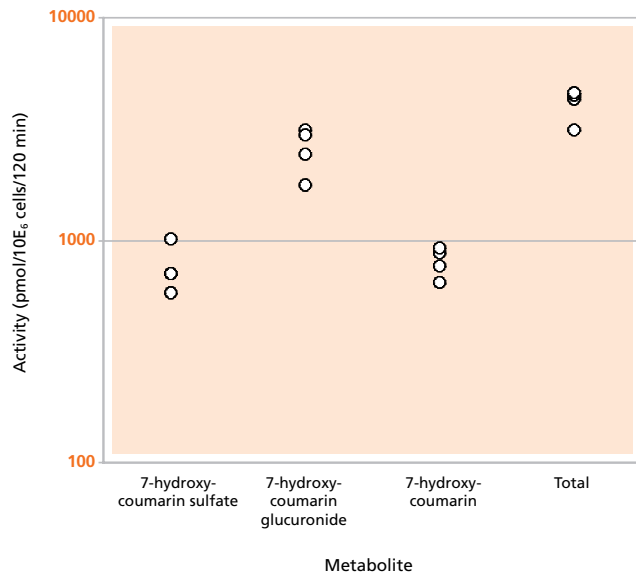
Time course of ethoxycoumarin metabolism in a 10-donor pool of single freeze, cryopreserved hepatocytes showing the expected linearity in formation of metabolites.

HISTORICAL ASSAY PERFORMANCE FOR METABOLIC STABILITY IN HUMAN, RAT, AND MOUSE LIVER MICROSOMES



In vitro intrinsic clearance results obtained for positive control compounds in human (HLM), rat (RLM), and mouse (MsLM) liver microsomes. Boxes represent the 25th- 75th percentile, the line marks the median, error bars indicate the 90th and 10th percentiles. Data was obtained using multiple lots of microsomes.

INTERDAY REPRODUCIBILITY OF ETHOXYCOUMARIN METABOLISM



Metabolism of 50 μ M ethoxycoumarin by a 10-donor pool of human cryopreserved hepatocytes. Values represent means of duplicate determinations on 4 independent days.

BD GENTEST PRODUCT HIGHLIGHTS

BD Biosciences Study Directors have immediate access to high-quality BD products for conducting studies, including BD Gentest™ HLMs, hepatocytes, chemicals and BD Supersomes™, the industry gold standard for recombinant enzymes and the full portfolio of BD cell culture products - enabling trusted science and reliable results.

BD GENTEST™ CRYOHEPATOCYTES

BD Gentest metabolism-qualified human cryohepatocytes are suitable for in vivo like metabolic stability and drug clearance studies. Every lot is extensively tested for phase I and II metabolic activities.

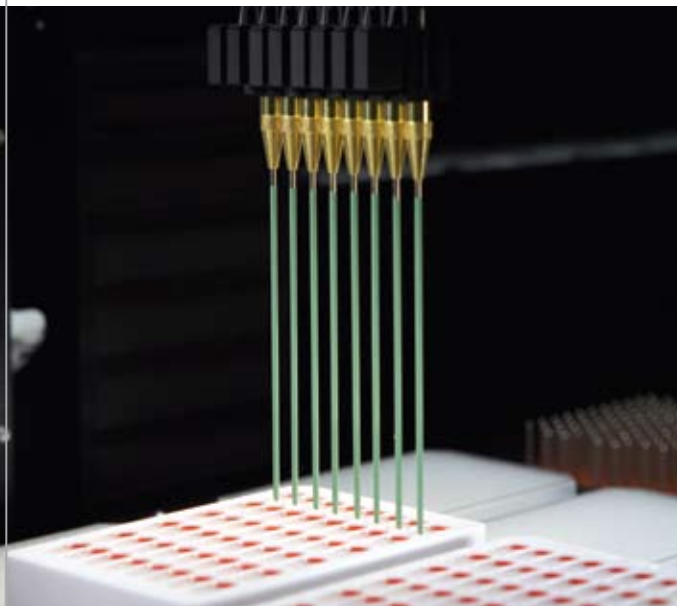
BD ULTRAPOL™ HLM 150

BD Biosciences recently launched BD UltraPool HLM 150, the first commercially available large donor pool. This donor pool of 150 donors is statistically modeled to provide researchers with a high degree of lot-to-lot consistency for CYP and UGT enzyme activity and naturally represents the "average patient" and known CYP polymorphisms.

BD SUPERSOMES™

BD Supersomes enzymes have been validated by multiple laboratories for well over a decade, providing consistent batch-to-batch performance and the widest selection of enzymes. Assays are qualified for 35 human and rat BD Supersomes enzymes. Human cytochrome P450 BD Supersomes enzymes are formulated with P450 enzyme, human cytochrome P450 oxidoreductase, and human cytochrome b5 to deliver optimal performance.

PROTEIN BINDING expertise

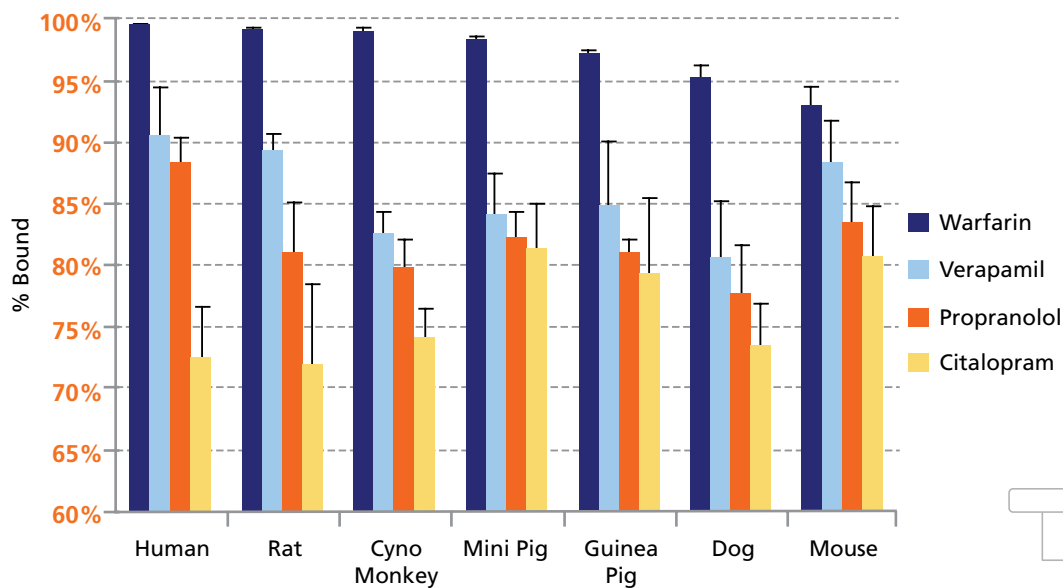


PLASMA PROTEIN BINDING USING RAPID EQUILIBRIUM DIALYSIS.

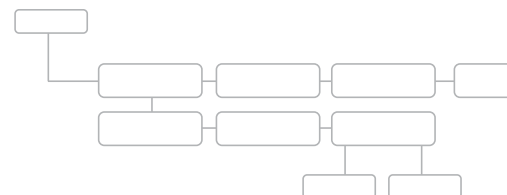
Assessment of plasma protein binding by rapid equilibrium dialysis applies the gold standard equilibrium dialysis technique to a high throughput discovery setting to accurately determine the bound and unbound fractions of a test article in human or animal plasma. BD Biosciences conducts PPB assays by rapid equilibrium dialysis with LC/MS/MS quantitation which provides a cost-effective screening of large numbers of compounds and fast turnaround times.

Results obtained at BD Biosciences using rapid equilibrium dialysis in human plasma are consistent with data reported in the literature. Results are highly reproducible over extended periods of time using various lots of plasma.

COMPARISON OF PROTEIN BINDING OF COMPARATOR COMPOUNDS IN HUMAN AND ANIMAL PLASMA



Comparison of mean % bound values across seven species at 10 μ M final concentrations. Data represent the means of replicates ($N \geq 5$) with standard deviations as error bars.



PROTEIN BINDING IN HUMAN PLASMA COMPARED WITH LITERATURE VALUES

| Compound | P E R C E N T B O U N D | |
|---------------|---------------------------|---------------|
| | Literature | Experimental |
| Amitriptyline | 95% | 95.4% (0.48%) |
| Atenolol | 6-16% | 4.0% (16.40%) |
| Bumetanide | 93% | 98.9% (0.19%) |
| Carbamazepine | 76% | 83.9% (3.85%) |
| Erythromycin | 84% | 79.1% (4.96%) |
| Haloperidol | 92% | 90.8% (1.20%) |
| Imipramine | 89-92% | 91.9% (0.89%) |
| Ketoprofen | >99% | 99.6% (0.17%) |
| Metoprolol | 12% | 3.5% (32.00%) |
| Naproxen | 99% | 95.3% (1.73%) |
| Propranolol | 81-93% | 83.2% (3.95%) |

| Compound | P E R C E N T B O U N D | |
|--------------|---------------------------|----------------|
| | Literature | Experimental |
| Terfenadine | 97% | 99.5% (0.30%) |
| Warfarin | 99% | 99.5% (0.08%) |
| Furosemide | 91-99% | 89.8% (1.23%) |
| Tolbutamide | 96% | 98.9% (0.36%) |
| Verapamil | 90% | 92.9% (1.83%) |
| Thioridazine | >95% | 99.9% (0.04%) |
| Tacrine | 75% | 63.3% (6.21%) |
| Nadolol | 30% | 25.3% (8.11%) |
| Linezolid | 31% | 49.0% (15.60%) |
| Citalopram | 80% | 63.0% (2.58%) |

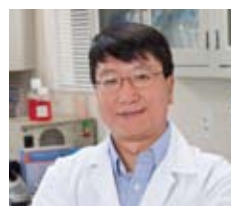
Comparison of % bound values obtained at BD Biosciences using rapid equilibrium dialysis in human plasma with literature data. Experimental values are means of replicates (N ≥ 4) with standard deviations in parentheses. Majority of literature values were collected from www.RXlist.com.



David Stresser

PROGRAM MANAGER

Dr. David Stresser has over 11 years experience in his current role, including services as a Study Director in the areas of CYP inhibition, induction and metabolism. Previously, David was a post-doctoral associate at the University of Massachusetts Medical School in Worcester, MA in the Department of Pharmacology and Molecular Toxicology. David received a Ph.D. in Toxicology from Oregon State University. He has been an invited speaker at various international meetings and universities and is a regular instructor at the High-Throughput Drug Metabolism/Disposition course co-sponsored by EUFAPS. Most recently, he organized a short course covering in vitro ADME methods sponsored by the Society for Biomolecular Screening (Lille, France 2009). Dr. David Stresser holds a patent entitled "Use of fluorescein aryl ethers in high throughput cytochrome P450 inhibition assays" and has authored and co-authored 31 articles in the field of drug metabolism.



George Zhang

STUDY DIRECTOR

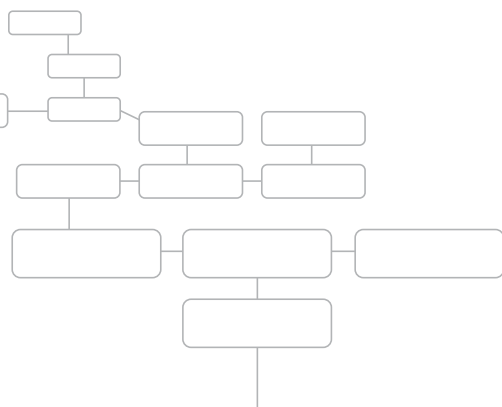
With over 15 years of research experience, Dr. George Zhang's expertise spans the areas of drug metabolism, enzyme induction and toxicity using in vitro models such as human hepatocytes. Prior to joining BD Biosciences, George investigated oxidative stress-induced hepatocyte toxicity and cytoprotection as an Assistant Research Professor in the Department of Pharmaceutical Sciences at Washington State University. He received his Ph.D. in Pharmacology and Toxicology from the University of Liverpool, UK where he studied nephrotoxicity and its antidotes. George also completed additional post-doctoral training on oxidative stress in myocardial ischemia and reperfusion at the University of Leicester, UK, Department of Surgery. He has authored and co-authored over 35 peer-reviewed papers in the areas of cytochrome P450 induction, oxidative stress and cytoprotection.



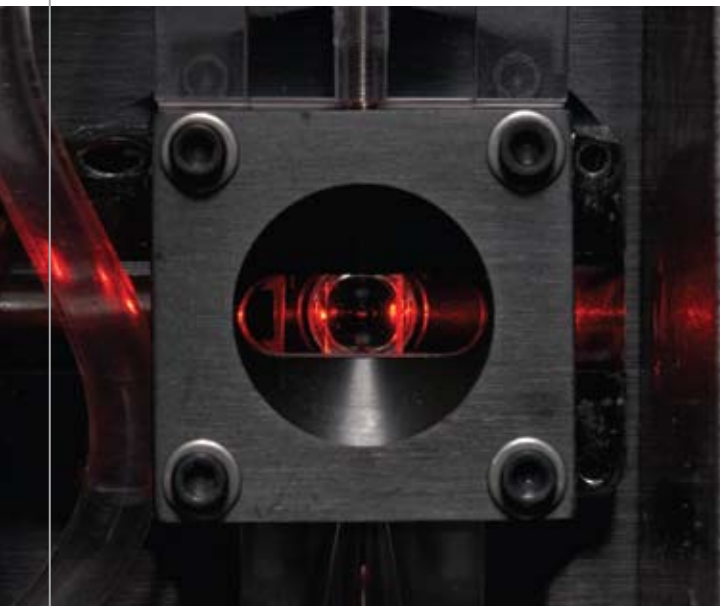
Shangara S. Dehal

STUDY DIRECTOR

Dr. Shangara S. Dehal has been a Study Director for BD Biosciences for more than 9 years. He directs projects in the areas of cytochrome P450 inhibition and induction, UGT inhibition, metabolic stability as well as cytochrome P450 and UGT reaction phenotyping studies. Prior to joining BD, Shangara completed postdoctoral training in Microbiology/Biochemistry in the Department of Biochemistry/Biophysics at the Max-Planck Institute for Biophysics in Frankfurt, Germany and also in the laboratory of Dr. David Kupfer at Worcester Foundation for Biomedical Research/University of Massachusetts Medical Center. As a Research Instructor, Shangara studied the metabolism of the insecticide methoxychlor and tamoxifen, an anti-breast cancer agent. He received his B.S. in Biochemistry from Hull University, UK, M.S. in Medicinal Chemistry and Ph.D. in Organic Chemistry/Biochemistry from Loughborough University, UK. Dr. Shangara S. Dehal has authored and co-authored more than 25 articles in peer-reviewed journals.



SOLUBILITY AND AGGREGATE DETECTION expertise



SOLUBILITY AND AGGREGATE DETECTION USING FLOW CYTOMETRY-BASED DETECTION.

Poor aqueous solubility and compound aggregation can impact the amount of compound available in bioassays. BD Biosciences provides evaluation of compound precipitation patterns via a flow cytometry-based detection method using the BD Gentest™ solubility scanner^[1]. The solubility scanner method permits testing in biological buffers to mimic the in vitro screening environment to provide assay relevant solubility data. When drug compounds aggregate, they often inhibit enzymes in a non-specific manner, creating false positive behavior^[2,3]. The BD Gentest solubility scanner is optimized for highly sensitive, reproducible scatter detection of compound aggregates and precipitates, providing flexibility to rule out false positive leads from screens early in the drug discovery process. Samples are analyzed at a rate of ~ 8 seconds per well, permitting fast turnaround of data in one to two weeks.

COMPARISON OF SOLUBILITY VALUES OBTAINED BY HPLC/UV AND FLOW WITH SELECTED LITERATURE VALUES

| Compound | EXPERIMENTAL SOLUBILITY (μM) | | |
|---------------------|------------------------------|-------------------|------------|
| | LC/UV | Flow ¹ | Literature |
| Amiodarone HCl | 0.0 | < 0.2 | – |
| Benzo(b)fluorene | 0.0 | < 0.2 | 0.1 |
| Danazol | 0.0 | 28.2 | 29 |
| Haloperidol | 0 (44) | 46.9 | 37.2 |
| Pyrene | 0.0 | 0.6 | 0.6 |
| Quintozene | 0.0 | 2.3 | 1.4 |
| Trifluralin | 0.0 | 0.3 | 0.5 |
| Dinitramine | 7.2 | 37.5 | 3.4 |
| Progesterone | 29.0 | 46.9 | 28 |
| Pheny Isalicylate | 47.7 | 70 | 700 |
| Disulfiram | 51.4 | 70 | 13.7 |
| Bendroflumethiazide | 53.3 | 46.9 | 256 |
| Spironolactone | 69.3 | 70 | 53 |
| Benzthiazide | 124.6 | 93.8 | 25.7 |
| Prednisone | 351.9 | 187.5 | 870 |
| Hydroflumethiazide | 586.2 | >250 | 1109 |
| Butamben | 598.3 | >250 | 1730 |
| Benzocaine | >600 | >250 | 7930 |
| Butylparaben | >600 | >250 | 1066 |

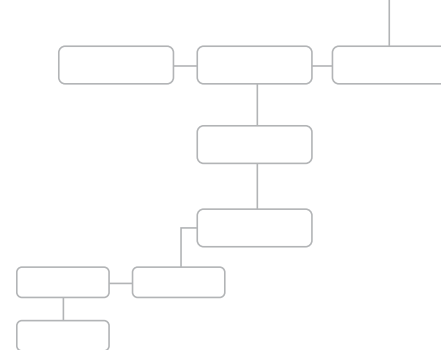
| Compound | EXPERIMENTAL SOLUBILITY (μM) | | |
|----------------|------------------------------|-------------------|------------|
| | LC/UV | Flow ¹ | Literature |
| Caffeine | >600 | >250 | |
| Chlorpromide | >600 | >250 | 932 |
| Fenbufen | >600 | >250 | |
| Flurbiprofen | >600 | >250 | |
| Furosemide | >600 | >250 | |
| Gemfibrozil | >600 | >250 | |
| Hydrocortisone | >600 | >250 | 833 |
| Hydroquinine | >600 | 175 | 888 |
| Iodipamide | >600 | 175 | |
| Ketoprofen | >600 | >250 | |
| Metoprolol | >600 | >250 | |
| Morin hydrate | >600 | 18.75 | |
| Naproxen | >600 | >250 | |
| Nitrofurazone | >600 | 175 | 1060 |
| Phenylbutazone | >600 | >250 | |
| Propranolol | >600 | >250 | |
| Proylparaben | >600 | >250 | |
| Tolazamide | >600 | >250 | 210 |

[1] Goodwin, J.J. Rationale and benefit of using high throughput solubility screens in drug discovery. Drug Discovery Today:Technologies 3:67 (2006).

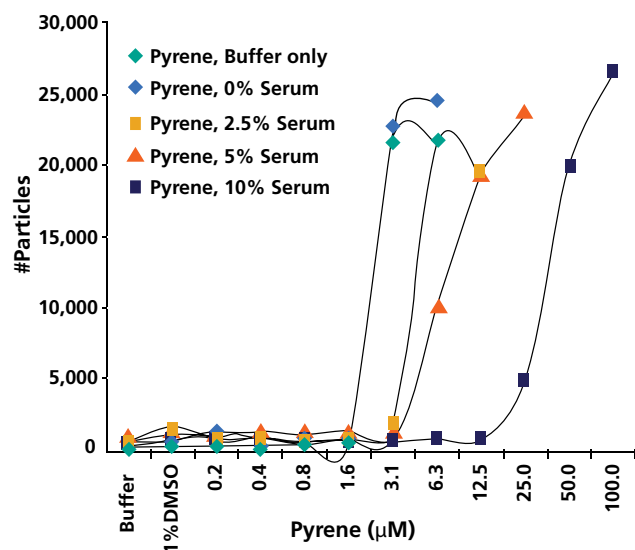
[2] Seidler, J., et al. Identification and Prediction of Promiscuous Aggregating Inhibitors among Known Drugs. J. Med. Chem.46:4477 (2003).

[3] McGovern, S.L. et al A common mechanism underlying promiscuous inhibitors from virtual and high-throughput screening. J. Med. Chem., 45:1712 (2002).

[1] Values represent the range obtained using the solubility scanner for replicates obtained on 4 independent days



SOLUBILITY OF PYRENE IN CULTURE MEDIUM WITH 0, 2.5, 5, OR 10% FBS



The BD Gentest™ solubility scanner can be used to measure differences in compound solubility as a function of serum concentration. This graph demonstrates that fewer pyrene particles are detected by the BD Gentest solubility scanner as serum concentration increases, reflecting the decrease in pyrene precipitation as serum is added.



Joe Goodwin

STUDY DIRECTOR

Joe Goodwin has more than 10 years in cell biology and cancer therapy research including an emphasis in solubility instrumentation and application development for drug discovery and research markets. Joe also has 4 years experience as Project Leader and Study Director for Solubility and Aggregation studies. With a B.S. in Biology and as a Certified Flow Cytometrist, Joe has used his expertise to develop instrumentation and applications for solubility and aggregate detection. With exceptional attention to detail, Joe adds insight and value to the studies he directs for clients, enabling clear results transmission and unparalleled abilities to analyze complex data from various methods and integrate into a cohesive conclusion.

ADVANCED TECHNOLOGY

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The *in vitro* ADME market leader in P450 products and services, BD Biosciences, and the technology leader in high-throughput mass spectrometry, BIOCIUS Life Sciences, are combining expertise to provide a novel mass spectrometry-based, high-throughput complete service package for cytochrome P450 inhibition - providing you with a high-quality, cost-effective inhibition screening service.

BD GENTEST SOLUBILITY SCANNER

The BD Gentest solubility scanner method permits testing in biological buffers to mimic the *in vitro* screening environment to provide assay relevant solubility data. The solubility scanner is optimized for highly sensitive, reproducible scatter detection of compound aggregates and precipitates, providing flexibility to rule out false positive leads from screens early in the drug discovery process.

LARGE PORTFOLIO OF ENZYMES, CHEMICALS, METABOLITE STANDARDS

Understanding how a drug compounds' enzymatic metabolic pathways and metabolic rates influence its clearance, metabolite concentration, and potential drug-drug interactions is a critical component to developing safe and effective drugs. BD Biosciences extensive portfolio of products and services to support the characterization of drug metabolism and drug-drug interactions include: recombinant drug metabolizing enzymes, human- and animal-derived hepatocytes and tissue fractions, antibodies, chemical substrates, metabolites and inhibitors needed to perform metabolic studies.

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