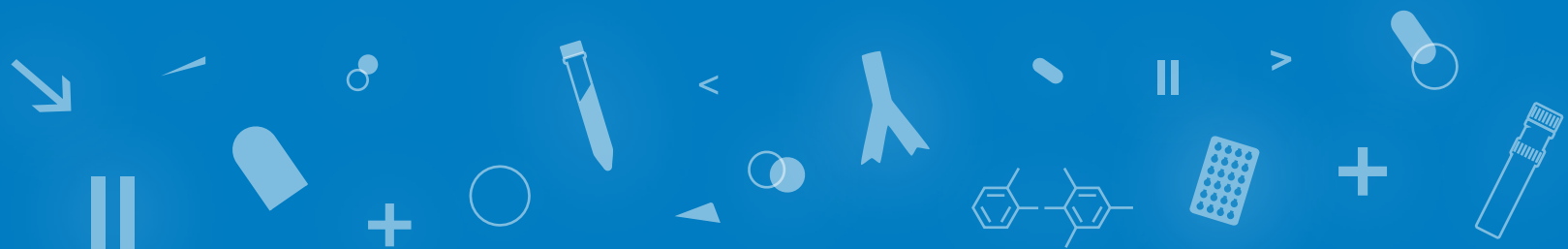
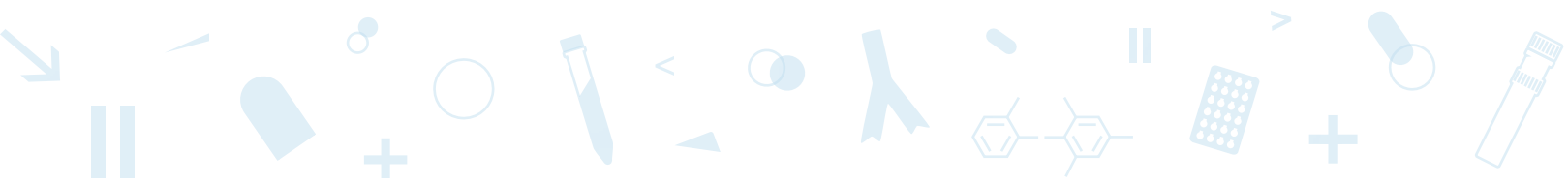




Helping all people
live healthy lives

BD GentestSM Contract Research Services





Partners in the search for new drugs

Introduction

BD GentestSM Contract Research Services

BD Gentest Contract Research Services has over 15 years experience developing *in vitro* services to support pharmaceutical drug discovery and development programs in the early ADME/Tox phase. Our Study Directors are highly skilled scientists with in-depth knowledge of absorption and transport, metabolism, and toxicity. This expertise gives BD Biosciences Study Directors the ability to partner with you to develop and deliver a broad range of *in vitro* ADME/Tox studies to meet your discovery and development project needs. We ensure the highest level of quality standards and adhere to current regulatory requirements and applicable FDA-sponsored guidance documents.

Utilizing state-of-the art techniques and equipment, BD Biosciences is able to assist our clients in screening for viable drug candidates during drug discovery or to prepare regulatory agency submission-quality reports for your drug development compounds. Let our team of experts take you to the next level with studies designed to predict drug-drug interactions and human pharmacokinetics using BD Gentest's innovative *in vitro* products, cell models, and methodologies.

Acronyms

7-BQ: 7-Benzyloxyquinoline	BzRes: 7-Benzyloxyresorufin	OCT: Organic cation transporter
7-MFC: 7-Methoxy-4-trifluoro-methyl-Coumarin	CEC: 3-Cyano-7-ethoxycoumarin	OMF: 3-O-Methylfluorescein
ABC: ABC-binding cassette	EFC: 7-Ethoxy-4-trifluoro-methyl-Coumarin	PB: Phenobarbital
ACE: Angiotensin converting enzyme	GLP: Good Laboratory Practice	P-gp: P-glycoprotein
AMMC: 3-[2-(N,N-diethyl-N-methylamino)ethyl]-7-methoxy-4-methyl-Coumarin	HLM: Human liver microsome	PEPT: Proton oligopeptide co-transporter
AZA: Azamulin	KTZ: Ketoconazole	RIT: Ritonavir
AZT: Azidothymidine	MAMC: 7-Methoxy-4-amino methyl-Coumarin	RT-PCR: Real-time reverse-transcription polymerase chain reaction
BCRP: Breast cancer resistance protein	MRP: Multidrug resistance-associated protein	SLC: Solute-linked carrier
BCS: Biopharmaceutics Classification System	NCE: new chemical entity	TEA: Tetraethylammonium
BFC: 7-Benzyloxy-4-trifluoro-methyl-Coumarin	NTCP: Sodium taurocholate co-transport protein	TDI: Time-dependent inhibition
BSEP: Bile salt export pump	OAT: Organic anion transporter	UGT: UDP-glucuronosyl transferases
	OATP: Organic anion transporting polypeptide	

Ordering Information

United States

BD GentestSM Contract Research Services

To discuss and order BD Gentest Contract Research Services, contact BD Biosciences at:

tel: 888.334.5229 x2246 or
781.935.5115 x2246

Technical Support

Contact a BD Biosciences Technical Support Representative at:

tel: 877.232.8995 or 978.901.7389

Monday through Friday

9:00 a.m. – 6:00 p.m. Eastern Time

fax: 978.901.7491

e-mail: admetox@bd.com

International

Orders for BD GentestSM Contract Research Services, should be placed with your regional BD Biosciences office or contact BDBCcustomerService@bd.com for further details.

Protein Binding Studies

Protein Binding Services

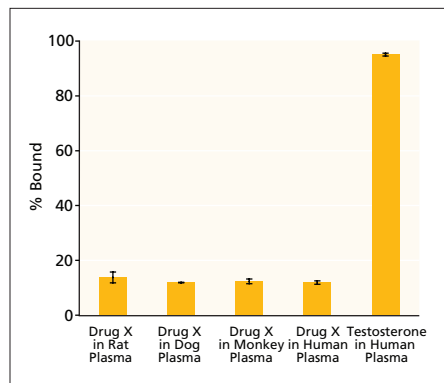
- Equilibrium Dialysis
- Blood Cell Partitioning
- Ultrafiltration
- High throughput drug discovery applications
- Drug development applications

Custom Designed Studies

Introduction

Drug efficacy and disposition are influenced by binding of a drug to plasma proteins, primarily serum albumin and α -acid glycoprotein.¹ High drug-protein binding can both reduce the fraction of free drug available for target sites and prolong the duration of drug activity.² BD Biosciences provides rapid *in vitro* plasma protein binding testing, offering both ultrafiltration and equilibrium dialysis methods to determine % drug bound to plasma proteins. Blood cell partitioning testing to determine the % drug associated with blood cells is also available. A standard set of test compound concentrations and incubation times may be used. Appropriate positive controls are included. Incubations can be performed with radiolabeled and non-radiolabeled compounds, with samples analyzed by LC/MS or radiometric detection. These services are available with human, rat, mouse, monkey, dog, and rabbit plasma and blood, and can be conducted according to GLP regulations.

Drug-Plasma Protein Binding Results Obtained in Multiple Species Plasma Using Ultrafiltration



Drug-plasma protein binding results from Ultrafiltration assays using rat, dog, cynomolgus monkey, and human plasma fortified with test drug X or testosterone. Results are the mean and standard deviation of triplicate determinations.

Comparison Sample Test Data for BD Gentest™ Plasma Protein Binding Data

Compound	Literature Values % Bound to Plasma Protein	BD Gentest Values						
		Equilibrium Dialysis		Blood Cell Partitioning		Ultrafiltration		
		% Bound to Plasma Protein	% Mass Balance	% Associated with Blood Cells	Cb/Cp Ratio	% Non-Specifically Bound	% Bound to Plasma Protein	% Mass Balance
Testosterone	95	94.1	93.5	27.8	0.65	1.3	95.1	98.6
Salicylic Acid	82	81.9	86.6	8.7	0.49	0.2	83.0	96.6
Example Drug X	—	10.4	90.1	41.3	0.92	0.1	10.5	101.7

References

1. Lin, J., et al. The role of Absorption, Distribution, Metabolism, Excretion and Toxicity in Drug Discovery. *Current Topics in Med. Chem.* **3**:1125 (2003).
2. Kratochwil, N.A., et al. Predicting plasma protein binding of drugs: a new approach. *Biochem. Pharmacol.* **64**:1355 (2002).



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BD Falcon™

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