

HIGH THROUGHPUT REACTION PHENOTYPING

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. BD's in-depth experience in this area using BD Supersomes™ enzymes, the gold standard for recombinant drug metabolizing enzymes, is a key element to delivering reproducible results. Only BD GentestSM 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.

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

BD SUPERSOMES ENZYMES PROVIDE HIGH-QUALITY DATA

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.

FLEXIBLE ASSAY DESIGNS

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.

DATA SUITABLE FOR RAPID-DECISION MAKING

Substrate loss analysis with BD Supersomes enzymes provides a high-throughput reproducible method to determine the metabolic role of an individual drug metabolizing enzyme.

[More on reverse](#)

KEY FEATURES

- Provide results using BD Supersomes enzymes, the accepted "gold standard"
- Offers analysis with the widest selection of recombinant drug metabolizing enzymes
- Results delivered with a 1-2 week turnaround time

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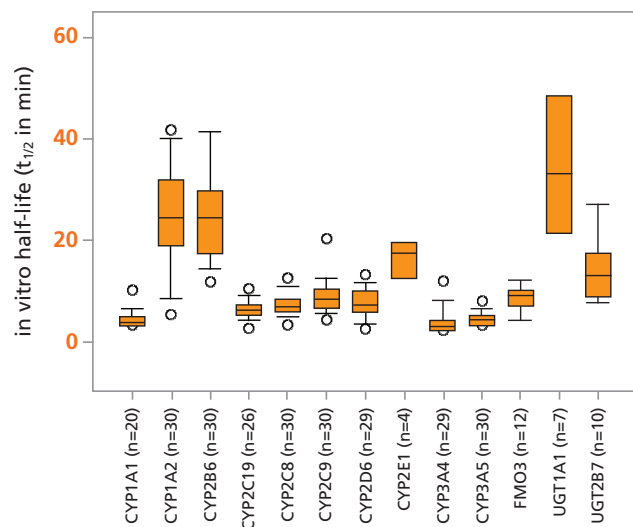
To inquire about BD GentestSM Contract Research Services, contact 888.334.5229 x2246 or 781.935.5115 x2246. Outside the U.S., visit bdbiosciences.com/offices to locate your nearest BD Biosciences office.



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SPECIFICATIONS:

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.

ADDITIONAL ENZYMES AVAILABLE WITH QUALIFIED POSITIVE CONTROLS FOR LOSS OF PARENT:

Enzyme	Substrate
CYP2J2	Terfenadine
CYP4F12	Terfenadine
CYP4F2	Leukotriene B4
CYP4F3A	Leukotriene B4
CYP4F3B	Leukotriene B4
FMO1	Benzylamine
MAO-A	Kynuramine
MAO-B	Kynuramine
UGT1A6	7-Hydroxy-4-trifluoromethylcoumarin
UGT1A9	7-Hydroxy-4-trifluoromethylcoumarin
Rat CYP1A1	Amodiaquine
Rat CYP1A2	Phenacetin
Rat CYP2A1	Testosterone
Rat CYP2A2	Testosterone
Rat CYP2B1	Testosterone
Rat CYP2C11	Testosterone
Rat CYP2C6	Diclofenac
Rat CYP2D1	Dextromethorphan
Rat CYP2D2	dextromethorphan
Rat CYP2E1	P-nitrophenol
Rat CYP3A1	Midazolam
Rat CYP3A2	Midazolam

STUDY DESIGN SUMMARY

TEST SYSTEM:	BD Supersomes.
PROTEIN CONCENTRATION:	Dependent on enzyme.
POSITIVE CONTROLS:	Suitable substrate for each enzyme.
NEGATIVE CONTROL:	Insect control BD Supersomes enzymes.
TIME POINTS:	4, non-zero.
ANALYTICAL METHOD:	LC/MS/MS.
CONCENTRATIONS:	Single test article concentration, in duplicate.
REPORT:	Percent loss, elimination rate constant, half-life Excel-based data report.

References

- [1] Youdim KA, Zayed A, Dickins M, Phipps A, Griffiths M, Darekar A, Hyland R, Fahmi O, Hurst S., Plowchalk DR, Cook J, Guo F & Obach RS (2008) Application of CYP3A4 in vitro data to predict clinical drug–drug interactions; predictions of compounds as objects of interaction. Br. J. Clin. Pharmacol. 65:680-92.
- [2] Williams JA, Hurst SI, Bauman J, Jones BC, Hyland R, Gibbs JP, Obach RS, Ball SE (2003) Reaction phenotyping in drug discovery: moving forward with confidence? Curr Drug Metab. 6:527-34
- [3] FDA Draft Guidance for Industry - Drug Interaction Studies – Study Design, Data Analysis, and Implications for Dosing and Labeling (September 2006).