

**Evaluation of the Interplay between Uptake Transport and CYP3A4 Induction in
Micro-patterned Co-cultured Hepatocytes**

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Drug Metabolism and Disposition
Supplemental Data

Supplemental Table 1: Demographic Information of Human Hepatocyte Donors

Donor ID	Sex	Age (yr)	Race	Cause of Death	Medical History
Hu1624	F	72	Caucasian		Aspirin
BPB	F	42	Caucasian	Head Trauma	
NON	F	35	Caucasian	SIGSW ^a	Alcohol, Tobacco, IV drug abuse

^a SIGSW – self-inflicted gun-shot wound

Supplemental Table 2: Pharmacokinetic and Pharmacodynamic Properties of Perpetrator Compounds.

Compound	Plasma Protein Binding	Metabolism	Transporter Substrate	P _{app} (x10 ⁻⁶ cm/sec)	AUC (μg·hr/mL)	Cmax (μg/mL)	MDZ AUC Decrease (%)	Clinical Dose of Perpetrator	Reference
Rifampicin	89%	Rapid deacetylation by arylacetamide deacetylase (AADAC).	OATP1B1, OATP1B3, P-gP	1.4 ± 0.18	28.1	8.5	93	600 mg QD for 14 days	(Backman et al., 1996) (Niemi et al., 2006) (Nakajima et al., 2011) (Yamaguchi et al., 2011)
Bosentan	98%	Metabolized by CYP2C9 and CYP3A4 (and possibly CYP2C19)	OATP1B1, OATP1B3	1.1 ± 0.26	5.2	1.1	60.6 ^a	125mg BID for 10 days	(US Food and Drug Administration, 2001) (Treiber et al., 2007) (Burgess et al., 2008)
Phenytoin	90%	Up to 90% is metabolized by CYP2C19 and CYP2C9	P-gP	16.8 ± 6.88	191	10-20	94	300 mg QD	(Backman et al., 1996) (Schinkel et al., 1996) (Patsalos et al., 2002) (Lim et al., 2004)
Carbamazepine	75%	Metabolized by CYP3A4	P-gP	27.1 ± 4.21	NA	4.8-5.5	61 ^b	400 mg QD 28 days	(Otani et al., 1996) (Schlienger et al., 2000) (Sitsen et al., 2001) (Patsalos et al., 2002)

^a Sildenafil as substrate of CYP3A4, ^b Mirtazapine as substrate of CYP3A4, NA indicates that data was not available

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