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DATA SHEET

XTreme 200

Lot No. 0910312

Human Liver Microsomes
Pool of 200 (100 Male and 100 Female)
Suspension medium: 250 mM sucrose

H2610	**0.5 mL at 20 mg/mL**
H2620	**1.0 mL at 20 mg/mL**
H2630	**5.0 mL at 20 mg/mL**
H2640	**50.0 mL at 20 mg/mL**

Specific content and activities		**Content or Rate**
Cytochrome P450	(nmol/mg protein)	0.478
Cytochrome b_5	(nmol/mg protein)	0.369
NADPH-cytochrome *c* reductase	(nmol/mg protein/min)	162 ± 7

Enzyme	**Marker substrate reaction**	**[S] (µM)**	**Rate (pmol/mg protein/min)**
CYP1A2	Phenacetin *O*-dealkylation	80	534 ± 29
CYP2A6	Coumarin 7-hydroxylation	50	1090 ± 140
CYP2B6	Bupropion hydroxylation	500	538 ± 22
CYP2C8	Amodiaquine *N*-dealkylation	20	2710 ± 140
CYP2C9	Diclofenac 4'-hydroxylation	100	2310 ± 130
CYP2C19	*S*-Mephenytoin 4'-hydroxylation	400	78.6 ± 8.1
CYP2D6	Dextromethorphan *O*-demethylation	80	274 ± 11
CYP2E1	Chlorzoxazone 6-hydroxylation	500	1760 ± 130
CYP3A4/5	Testosterone 6β-hydroxylation	250	3910 ± 40
CYP3A4/5	Midazolam 1'-hydroxylation	30	750 ± 24
CYP4A11	Lauric acid 12-hydroxylation	100	1080 ± 70
FMO	Benzydamine *N*-oxygenation	500	776 ± 13
UGT1A1	17β-Estradiol 3-glucuronidation	100	1230 ± 20
UGT1A4	Trifluoperazine glucuronidation	25	1010 ± 50
UGT1A6	1-Naphthol glucuronidation	500	18800 ± 1500
UGT1A9	Propofol glucuronidation	50	5940 ± 250
UGT2B7	Morphine 3-glucuronidation	1000	3680 ± 240

Characterization is performed when the first lot of a product from a given subcellular fraction (*e.g., S9*) is prepared. Subsequent lots are subject to a verification test only. Values for enzyme activities were determined at a single substrate concentration and are mean ± standard deviation of three or more determinations.

To measure, cytochrome P450 (CYP) activity, liver microsomes (50 µg/mL) were incubated in triplicate at 37 ± 1°C for 10 minutes in potassium phosphate buffer (50 mM, pH 7.4), containing $MgCl_2$ (3.0 mM), EDTA (1.0 mM), NADP (1.0 mM), glucose-6-phosphate (5.0 mM), glucose-6-phosphate dehydrogenase (1 Unit/mL) and marker substrate, at the final concentrations indicated. Metabolite formation was determined by validated LC-MS/MS methods with deuterated metabolites as internal standards. FMO activity was measured under similar conditions except the protein concentration was 1 mg/mL and the buffer was 49 mM Tricine (pH 8.5).

To measure UDP-glucuronosyltransferase (UGT) activity, liver microsomes (10 - 250 µg/mL) were incubated in triplicate at 37 ± 1°C for 5 or 10 minutes in Tris-HCl (100 mM, pH 7.7 at 37°C), CHAPS (0.5 mM), EDTA (1.0 mM), $MgCl_2$ (10 mM), D-saccharic acid 1,4-lactone (100 µM), uridine diphosphate-glucuronic acid (8.0 mM) and marker substrate at the final concentrations indicated.

Each donor is equally represented in this pool.

Store at -80°C

For in vitro *use only*

CAUTION: *This sample should be considered as a potential biohazard and universal precautions should be followed.*

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DATASHEET PREPARED 11-MARCH-10

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Kinetic constants for CYP enzyme activities in human liver microsomes (pool of 200)

Enzyme	Marker substrate	Kinetic constants		
		Km (µM)	**Vmax** (pmol/mg protein/min)	**CL_{int}** (µL/mg protein/min)
CYP1A2	Phenacetin [S] range: 12-120 µM	**63.0 ± 4.1**	**820 ± 25**	**13.1 ± 1.2**
CYP2A6	Coumarin [S] range: 0.1-7.5 µM	**0.584 ± 0.165**	**877 ± 176**	**1580 ± 470**
CYP2B6	Bupropion [S] range: 10-500 µM	**76.5 ± 11.0**	**572 ± 94**	**7.49 ± 0.85**
CYP2B6	Efavirenz [S] range: 0.5-25 µM	**5.75 ± 0.13**	**136 ± 4**	**23.6 ± 0.5**
CYP2C8	Amodiaquine (high protein concentration) [S] range: 1-50 µM (low protein concentration) [S] range: 1-50 µM	**4.45 ± 0.48** **1.80 ± 0.16**	**2810 ± 91** **2450 ± 154**	**635 ± 63** **1360 ± 40**
CYP2C9	Diclofenac [S] range: 1.5-75 µM	**9.65 ± 0.58**	**2780 ± 101**	**288 ± 17**
CYP2C19	*S*-Mephenytoin [S] range: 8-400 µM	**49.6 ± 8.5**	**67.2 ± 3.6**	**1.38 ± 0.27**
CYP2D6	Dextromethorphan [S] range: 1.5-75 µM	**7.71 ± 2.63**	**223 ± 21**	**30.8 ± 8.6**
CYP2E1	Chlorzoxazone [S] range: 2-500 µM	**26.9 ± 3.8**	**1740 ± 25**	**65.3 ± 7.9**
CYP3A4/5	Testosterone [1] [S] range: 5-300 µM	**54.7 ± 11.3**[1]	**3500 ± 240**	**65.2 ± 8.2**[1]
CYP3A4/5	Midazolam [S] range: 1-50 µM	**2.52 ± 0.25**	**1160 ± 62**	**461 ± 21**
CYP4A11	Lauric acid [S] range: 0.3-15 µM	**2.41 ± 0.25**	**1190 ± 74**	**495 ± 29**

CL_{int}: Intrinsic clearance (i.e., Vmax/Km).

[1] For this assay, the Km column represents S_{50} (Hill coefficient = 1.3) and the CL_{int} column represents $CL_{max} = \frac{V_{max}}{S_{50}} \times \frac{(n-1)}{n(n-1)^{1/n}}$

Kinetic constants are mean ± standard deviation of three or more determinations.

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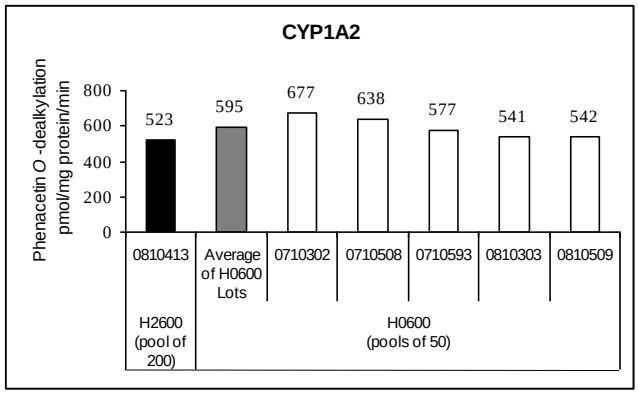
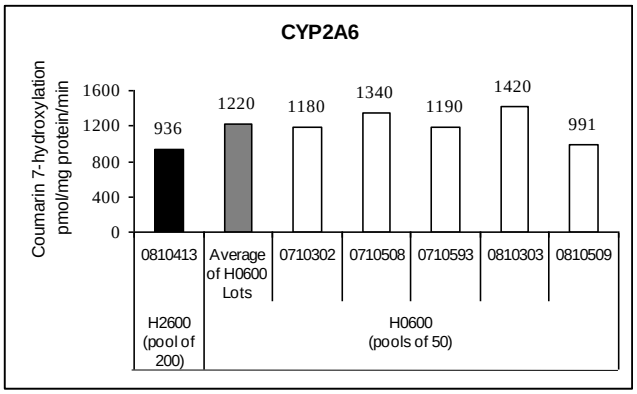
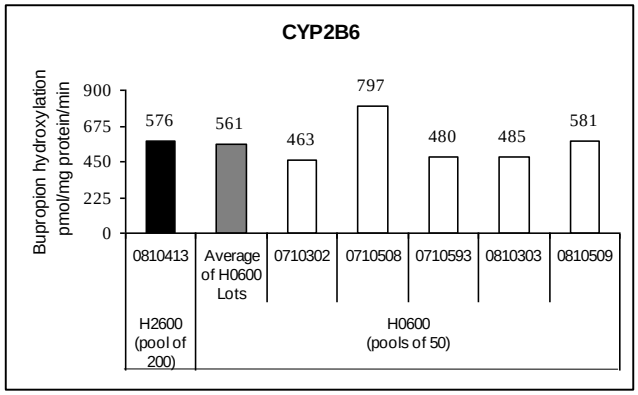
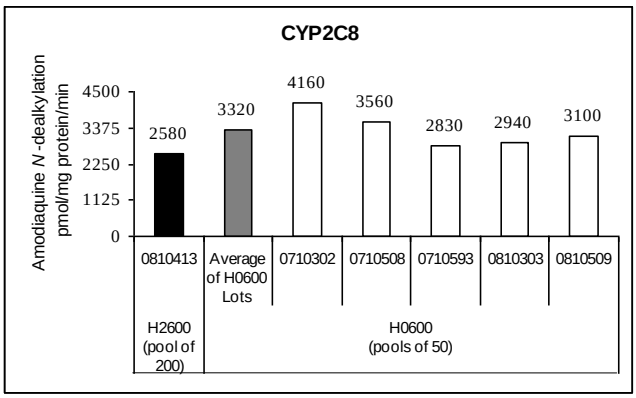
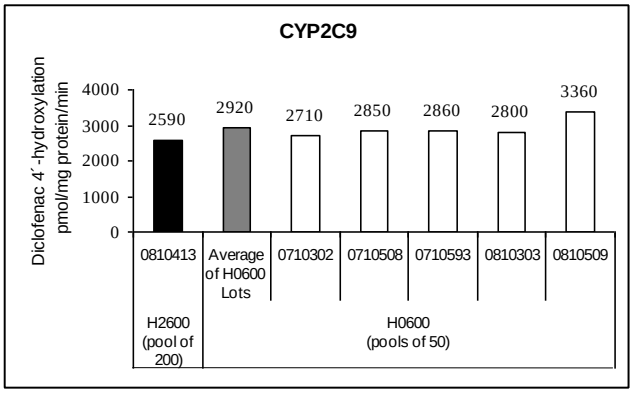
A comparison of H2600 (pool of 200) with previous pools of human liver microsomes (pools of 50)

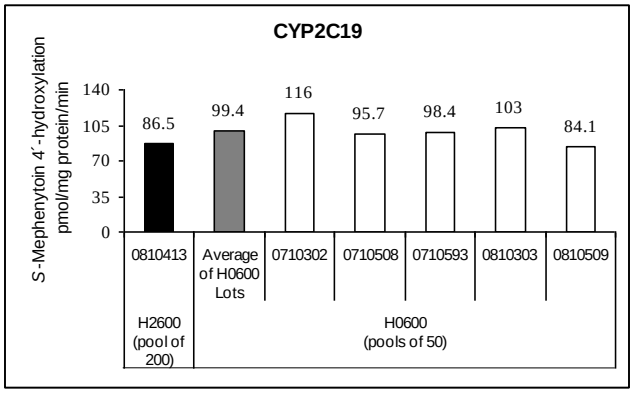












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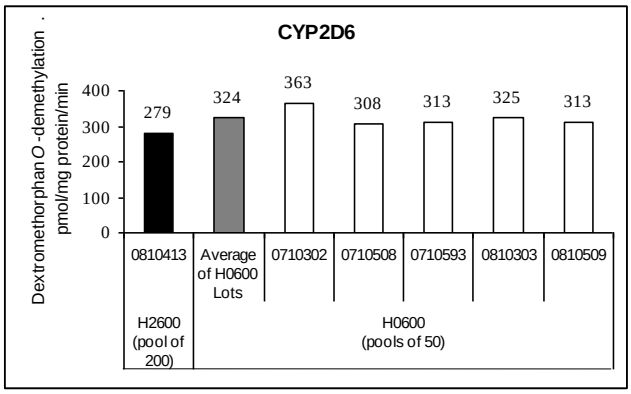

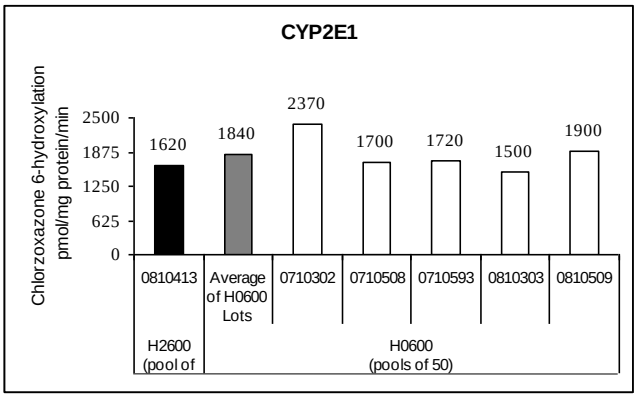

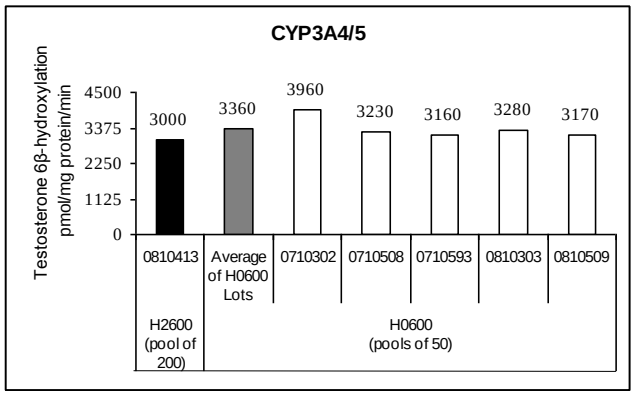

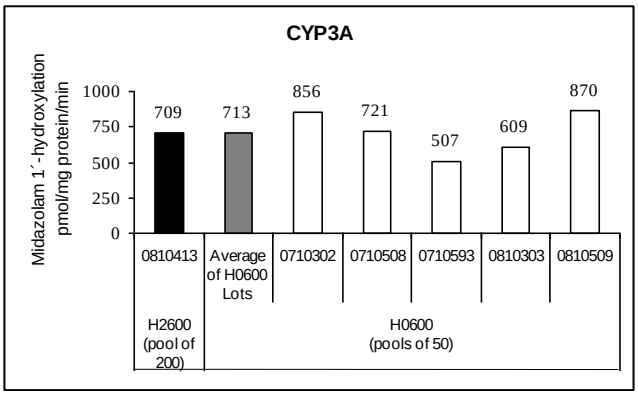

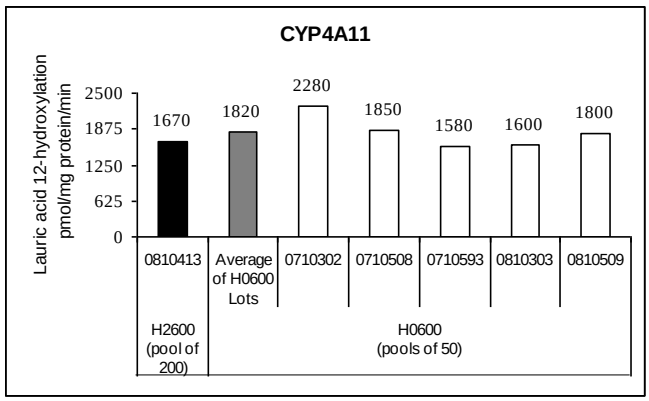

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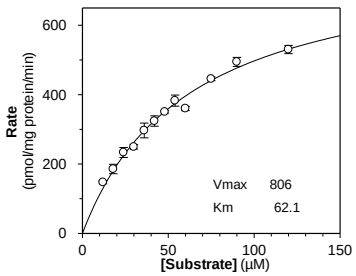
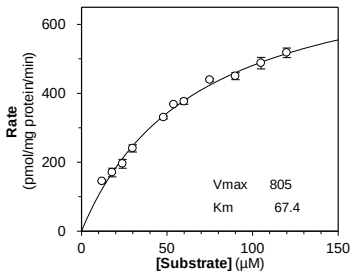
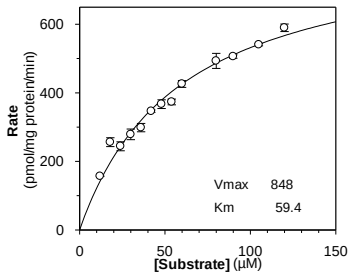
Km (µM) and Vmax (pmol/mg protein/min) determinations in human liver microsomes (Pool of 200)

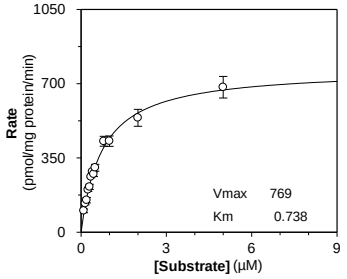
CYP1A2: Phenacetin *O*-dealkylation

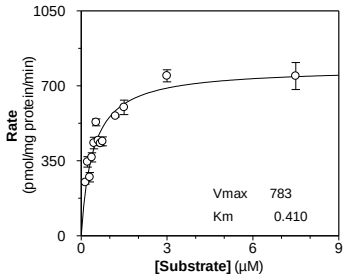


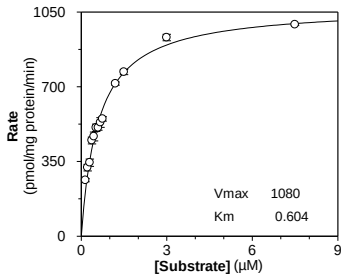




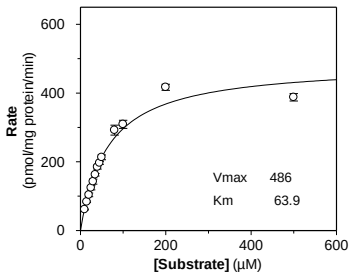
CYP2A6: Coumarin 7-hydroxylation

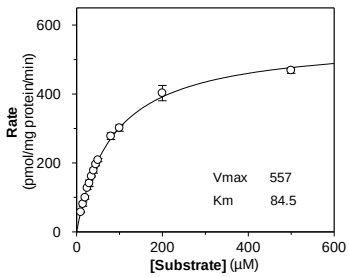


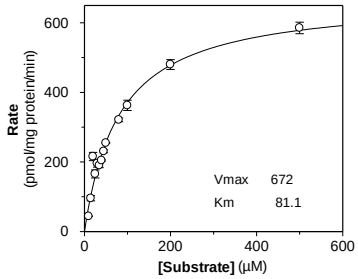




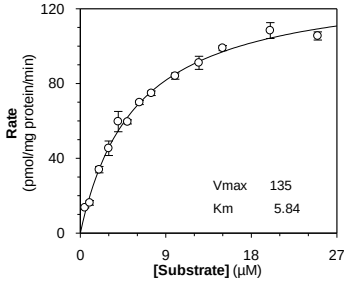
CYP2B6: Bupropion hydroxylation

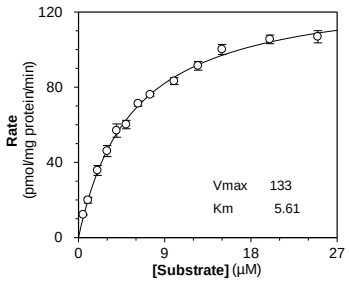


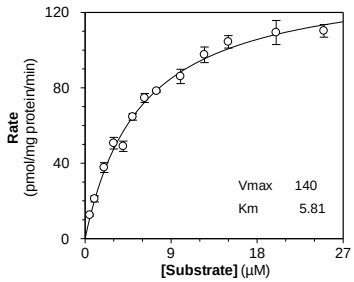




CYP2B6: Efavirenz 8-hydroxylation







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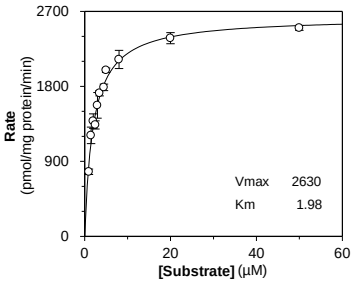
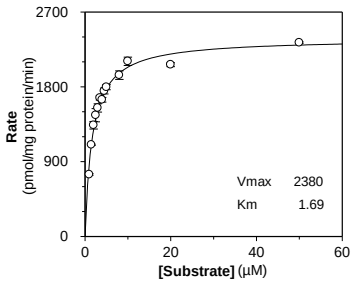
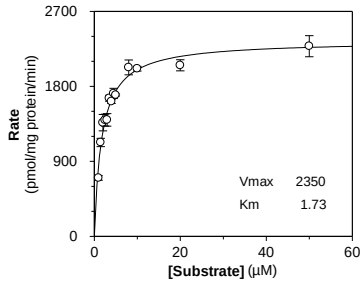
Km (µM) and Vmax (pmol/mg protein/min) determinations in human liver microsomes (Pool of 200)

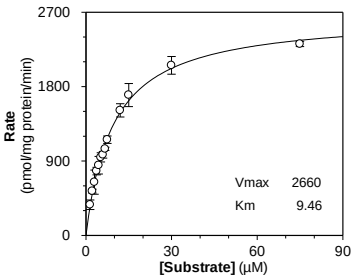
CYP2C8: Amodiaquine *N*-dealkylation

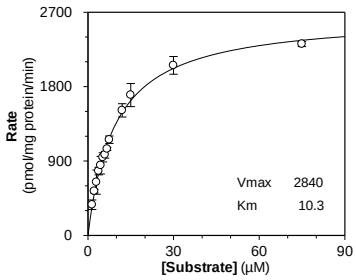


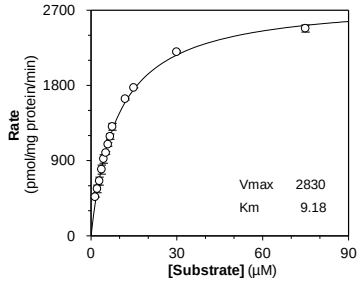




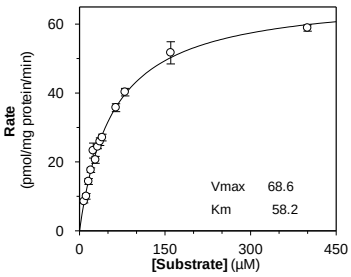
CYP2C9: Diclofenac 4´-hydroxylation

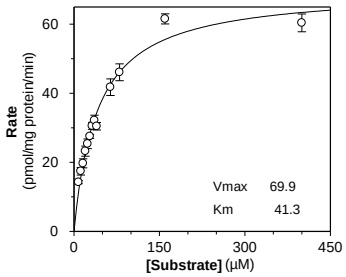


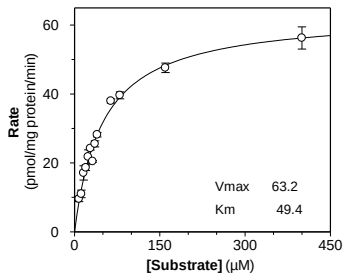




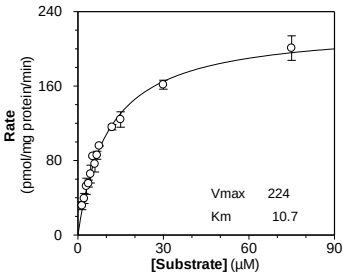
CYP2C19: *S*-Mephenytoin 4´-hydroxylation

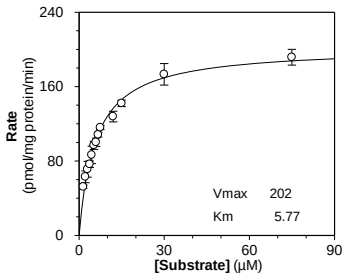


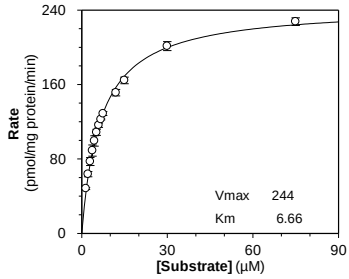




CYP2D6: Dextromethorphan *O*-demethylation







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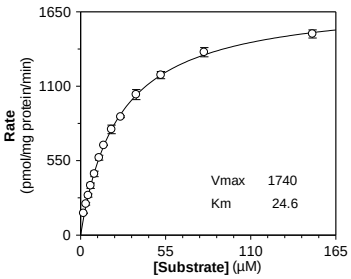
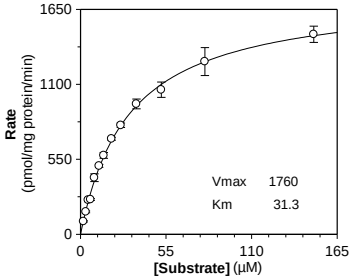
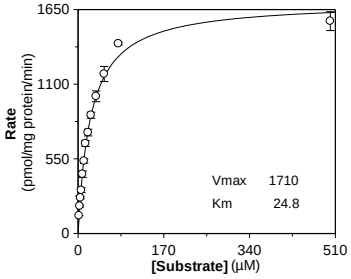
Km (µM) and Vmax (pmol/mg protein/min) determinations in human liver microsomes (Pool of 200)

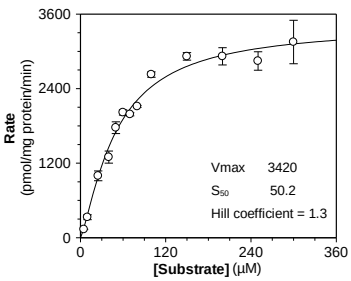
CYP2E1: Chlorzoxazone 6-hydroxylation

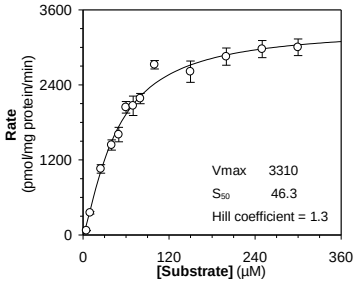


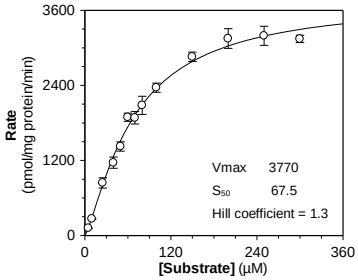




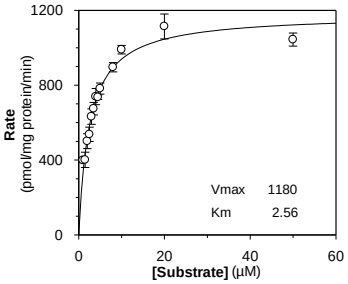
CYP3A4/5: Testosterone 6ß-hydroxylation

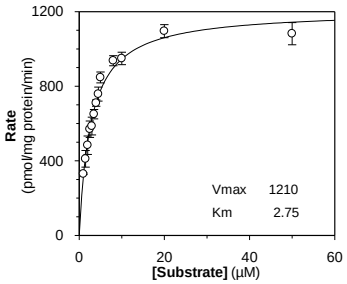


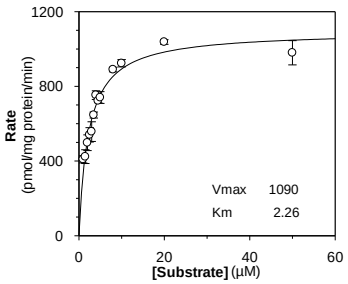




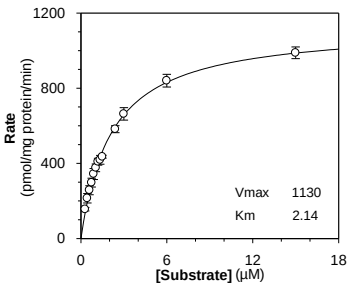
CYP3A4/5: Midazolam 1´-hydroxylation

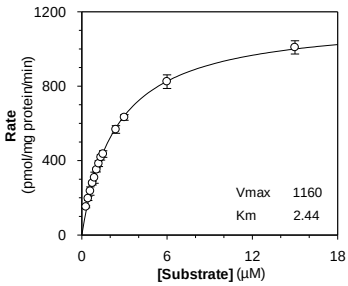


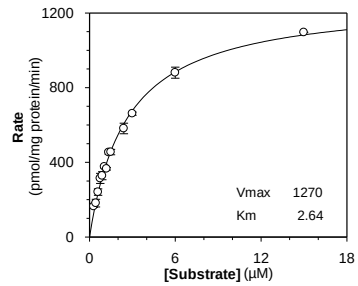




CYP4A11: Lauric acid 12-hydroxylation







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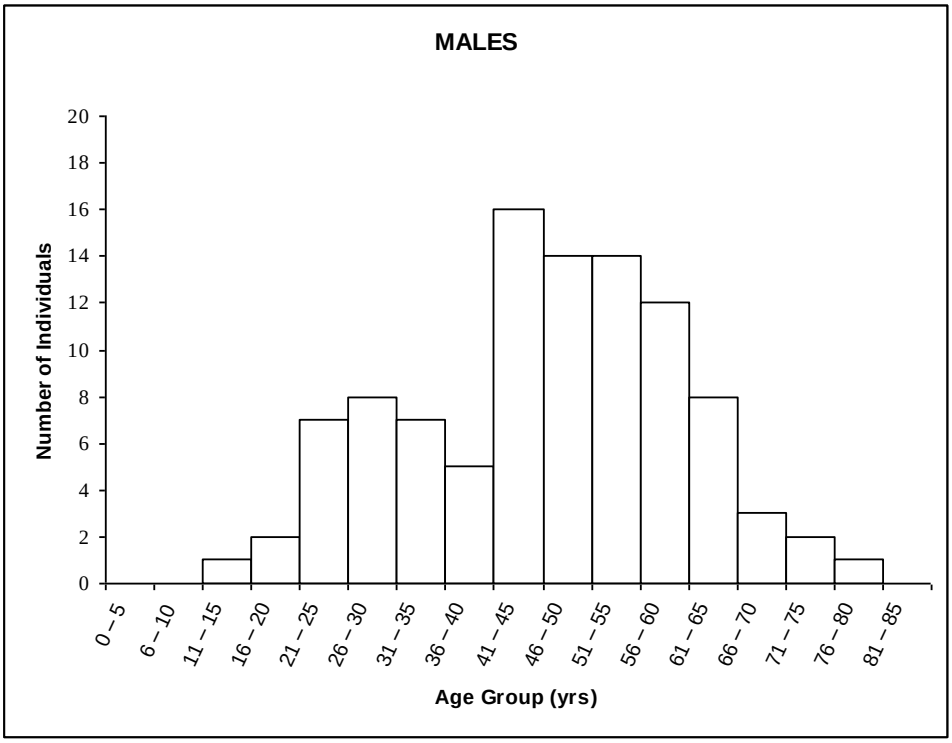
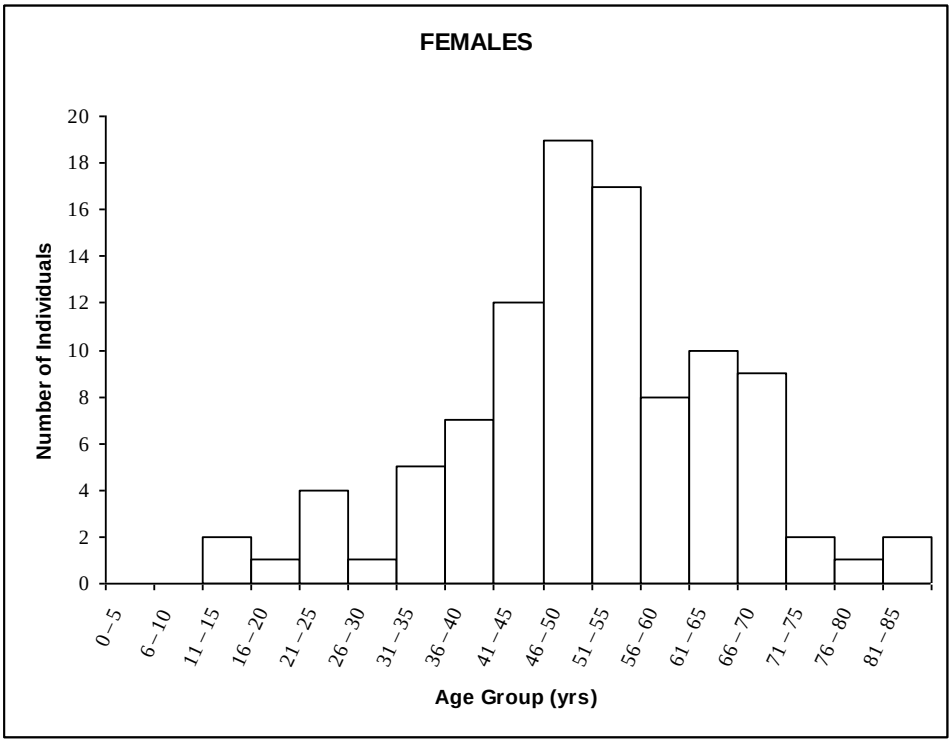
Age distribution of donors in the pool of 200





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Human Liver Microsomes

Donor Information for Human Liver Microsomes, Pool of 200

Sample	Gender	Age (Yrs)	Race	Cause of Death
248	M	29	Hispanic	Head trauma
253	M	57	Caucasian	Cerebrovascular accident
255	M	46	Hispanic	Anoxia
309	F	39	Caucasian	Cerebrovascular accident
325	M	54	Caucasian	Head trauma
337	F	57	Caucasian	Cerebrovascular accident
342	F	31	Caucasian	Anoxia
361	M	47	Caucasian	Head trauma
366	M	45	Hispanic	Anoxia
375	M	23	Caucasian	Head trauma
377	M	11	Caucasian	Anoxia
384	M	53	Caucasian	Anoxia
386	M	32	Caucasian	Head trauma
400	F	42	Caucasian	Anoxia
403	F	51	Caucasian	Anoxia
405	M	32	Caucasian	Anoxia
413	M	50	Caucasian	Anoxia
419	M	56	Hispanic	Cerebrovascular accident
427	M	22	Caucasian	Anoxia
444	F	43	Caucasian	Cerebrovascular accident
445	F	44	Asian	Cerebrovascular accident
476	F	46	Caucasian	Cerebrovascular accident
477	F	65	Caucasian	Anoxia
478	F	45	Caucasian	Anoxia
492	F	46	Hispanic	Cerebrovascular accident
506	F	48	Caucasian	Cerebrovascular accident
515	F	59	Caucasian	Cerebrovascular accident
517	F	47	Caucasian	Cerebrovascular accident
530	F	64	Caucasian	Head trauma
531	F	44	Caucasian	Cerebrovascular accident
536	F	34	Caucasian	Anoxia
540	F	54	Caucasian	Head trauma
542	F	53	Caucasian	Cerebrovascular accident
543	F	58	Caucasian	Anoxia
546	F	53	Caucasian	Cerebrovascular accident
550	F	68	Caucasian	Anoxia
554	F	43	Caucasian	Anoxia
556	F	49	Caucasian	Cerebrovascular accident
563	F	52	Caucasian	Cerebrovascular accident
564	F	42	Caucasian	Cerebrovascular accident
565	F	72	Caucasian	Cerebrovascular accident
571	F	45	Caucasian	Anoxia
573	F	47	Caucasian	Cerebrovascular accident
575	M	43	Caucasian	Head trauma
576	F	55	Caucasian	Cerebrovascular accident
577	F	23	Caucasian	Cerebrovascular accident
579	M	46	Caucasian	Cerebrovascular accident
580	M	77	Caucasian	Cerebrovascular accident

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Human Liver Microsomes

Donor Information for Human Liver Microsomes, Pool of 200

Sample	Gender	Age (Yrs)	Race	Cause of Death
581	M	63	African American	Cerebrovascular accident
582	F	60	Caucasian	Anoxia
583	M	64	Caucasian	Cerebrovascular accident
584	F	44	Caucasian	Head trauma
585	F	44	Caucasian	Anoxia
586	M	57	Caucasian	Anoxia
587	M	44	Caucasian	Cerebrovascular accident
588	M	29	Caucasian	Anoxia
589	F	55	Caucasian	Head trauma
590	F	64	Caucasian	Cerebrovascular accident
591	F	11	Caucasian	Head trauma
592	F	83	Caucasian	Head trauma
593	M	59	Caucasian	Head trauma
594	F	51	Caucasian	Cerebrovascular accident
595	M	37	Caucasian	Head trauma
597	M	41	Caucasian	Anoxia
598	M	55	Caucasian	Anoxia
599	M	51	Caucasian	Cerebrovascular accident
601	M	35	Caucasian	Anoxia
602	F	83	Caucasian	Cerebrovascular accident
603	F	67	Caucasian	Head trauma
605	F	49	Caucasian	Cerebrovascular accident
606	F	76	Caucasian	Cerebrovascular accident
607	M	52	Caucasian	Head trauma
608	F	54	Caucasian	Anoxia
609	F	48	Caucasian	Anoxia
611	F	25	Caucasian	Cerebrovascular accident
612	M	38	Caucasian	Anoxia
613	M	65	Caucasian	Cerebrovascular accident
615	M	55	Caucasian	Cerebrovascular accident
616	M	30	Caucasian	Head trauma
617	F	52	Caucasian	Cerebrovascular accident
618	F	70	Caucasian	Cerebrovascular accident
619	F	45	Caucasian	Cerebrovascular accident
620	M	48	Caucasian	Anoxia
621	M	50	Caucasian	Head trauma
622	M	41	Caucasian	Head trauma
623	F	69	Asian	Cerebrovascular accident
624	M	21	Caucasian	Anoxia
625	F	39	Caucasian	Anoxia
626	M	30	African American	Anoxia
628	F	62	Caucasian	Cerebrovascular accident
629	M	20	Caucasian	Anoxia
630	M	62	Caucasian	Cerebrovascular accident
631	M	24	Caucasian	Head trauma
632	M	57	Caucasian	Anoxia

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Human Liver Microsomes

Donor Information for Human Liver Microsomes, Pool of 200

Sample	Gender	Age (Yrs)	Race	Cause of Death
633	M	47	African American	Cerebrovascular accident
634	F	63	Caucasian	Cerebrovascular accident
637	F	66	Caucasian	Cerebrovascular accident
659	F	33	Hispanic	Anoxia
686	F	52	Caucasian	Anoxia
708	M	56	Caucasian	Head trauma
715	M	21	Caucasian	Head trauma
717	M	44	African American	Cerebrovascular accident
718	M	29	Caucasian	Head trauma
720	M	49	Caucasian	Head trauma
721	F	52	Caucasian	Cerebrovascular accident
723	F	57	Caucasian	Cerebrovascular accident
726	F	48	Caucasian	Cerebrovascular accident
728	M	39	Caucasian	Cerebrovascular accident
732	M	54	Caucasian	Head trauma
733	M	33	Caucasian	Anoxia
734	M	57	Caucasian	Cerebrovascular accident
735	M	34	Caucasian	Anoxia
736	F	46	Caucasian	Anoxia
737	F	49	African American	Anoxia
738	M	62	Caucasian	Cerebrovascular accident
739	M	66	Caucasian	Cerebrovascular accident
741	F	74	Caucasian	Head trauma
742	M	42	Caucasian	Head trauma
743	M	35	Caucasian	Cerebrovascular accident
745	M	59	Caucasian	Cerebrovascular accident
747	M	43	Caucasian	Anoxia
748	M	64	Caucasian	Cerebrovascular accident
750	F	53	Caucasian	Anoxia
751	M	29	Caucasian	Anoxia
752	M	44	Caucasian	Anoxia
754	F	66	Caucasian	Cerebrovascular accident
755	F	39	Caucasian	Anoxia
756	F	47	Caucasian	Cerebrovascular accident
757	M	54	Caucasian	Cerebrovascular accident
759	F	33	Caucasian	Cerebrovascular accident
760	M	44	Caucasian	Cerebrovascular accident
761	M	70	Caucasian	Cerebrovascular accident
763	F	53	Caucasian	Anoxia
765	F	39	Caucasian	Cerebrovascular accident
766	F	38	Caucasian	Anoxia
767	F	24	Caucasian	Cerebrovascular accident
768	F	63	Caucasian	Cerebrovascular accident
769	M	58	Caucasian	Head trauma
771	F	47	Hispanic	Anoxia
772	M	46	Caucasian	Anoxia

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Human Liver Microsomes

Donor Information for Human Liver Microsomes, Pool of 200

Sample	Gender	Age (Yrs)	Race	Cause of Death
773	M	46	Caucasian	Head trauma
774	M	55	Caucasian	Cerebrovascular accident
775	M	26	Caucasian	Head trauma
777	M	44	Hispanic	Head trauma
778	M	61	Caucasian	Cerebrovascular accident
779	F	20	Caucasian	Head trauma
780	F	48	African American	Cerebrovascular accident
781	F	15	Caucasian	Cerebrovascular accident
782	M	57	Caucasian	Cerebrovascular accident
783	M	41	Caucasian	Cerebrovascular accident
784	F	63	Caucasian	Head trauma
785	M	47	Caucasian	Head trauma
786	F	27	Caucasian	Head trauma
787	M	58	African American	Cerebrovascular accident
790	M	52	Caucasian	Cerebrovascular accident
794	M	36	Hispanic	Head trauma
795	M	69	Caucasian	Cerebrovascular accident
796	M	29	Caucasian	Anoxia
797	F	60	Caucasian	Cerebrovascular accident
798	M	55	Caucasian	Anoxia
800	F	67	Caucasian	Cerebrovascular accident
802	M	33	Caucasian	Cerebrovascular accident
803	M	23	African American	Head trauma
804	M	57	Caucasian	Cerebrovascular accident
805	F	24	African American	Anoxia
806	M	44	Caucasian	Head trauma
807	F	47	Caucasian	Cerebrovascular accident
809	M	51	Caucasian	Head trauma
810	M	37	Caucasian	Head trauma
811	M	16	Caucasian	Head trauma
812	M	73	Caucasian	Cerebrovascular accident
813	M	45	Caucasian	Anoxia
816	M	55	Hispanic	Head trauma
817	F	31	Caucasian	Anoxia
818	M	48	Hispanic	Cerebrovascular accident
819	F	49	Caucasian	Head trauma
820	F	65	Caucasian	Cerebrovascular accident
821	F	51	Caucasian	Anoxia
822	M	48	Asian	Cerebrovascular accident
823	F	67	Caucasian	Anoxia
824	M	74	Caucasian	Cerebrovascular accident
826	F	55	Caucasian	Cerebrovascular accident
827	M	54	Caucasian	Head trauma
829	M	45	Caucasian	Anoxia
830	M	65	Caucasian	Cerebrovascular accident
831	M	44	Caucasian	Anoxia
832	F	58	Caucasian	Cerebrovascular accident

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Human Liver Microsomes

Donor Information for Human Liver Microsomes, Pool of 200

Sample	Gender	Age (Yrs)	Race	Cause of Death
833	M	48	Hispanic	Anoxia
834	F	59	Caucasian	Cerebrovascular accident
835	M	23	Hispanic	Head trauma
847	F	55	Caucasian	Cerebrovascular accident
850	F	45	Caucasian	Anoxia
851	F	47	Caucasian	Cerebrovascular accident
858	F	69	Hispanic	Cerebrovascular accident
861	F	61	Caucasian	Head trauma
864	F	46	Caucasian	Cerebrovascular accident
867	F	39	Hispanic	Cerebrovascular accident
869	F	39	Hispanic	Cerebrovascular accident
874	F	65	Caucasian	Cerebrovascular accident
877	F	48	Caucasian	Cerebrovascular accident

Serology information

- Cytomegalovirus: 110 of 200 donors tested positive and 2 donors were not determined.
- RPR*: 198 donors tested negative and 2 donors were not determined
- HIV, HTLV, HbsAg, and HCV**: All donors tested negative.

* Rapid Plasma Reagin

** Antibody to Human Immunodeficiency Virus, Antibody to Human T Cell Lymphotropic Virus, Hepatitis Surface Antigen, Antibody to Hepatitis C Virus, respectively.

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