ABUNDANCE OF CYTOCHROMES P450 IN HUMAN LIVER: A META-ANALYSIS

K. Rowland Yeo[1], A. Rostami-Hodjegan[1,2] & G. T. Tucker[2]. [1]Simcyp Limited, Blades Enterprise Centre, John Street, Sheffield S2 4SU, UK and [2]Molecular Pharmacology & Pharmacogenetics, University of Sheffield, Royal Hallamshire Hospital, Sheffield S10 2JF, UK.

Recombinant systems expressing human cytochrome P450 isoforms (rCYP) are used *in vitro* for rapid screening for metabolic activity as well as for *in vitro in vivo* extrapolations (IVIVE) [1]. However, abundances of the respective enzymes in human liver are needed to correct for the relative contribution of each enzyme to the total metabolism. Shimada *et al.* (1994) is the most cited source for the latter information [914 citations in ISI database (September, 2003)] despite the fact that the study was based on liver samples from only 30 Japanese and 30 Caucasian subjects [2]. Therefore, the aim of our study was to derive abundance values for individual CYPs using all available data (19 sources).

Two electronic data bases MEDLINE and BIDS EMBASE, and personal files (1990-2003) containing references from Current Contents and Reference Update were searched for the pertinent literature using appropriate key words. Authors were contacted directly when further information was required. Only human liver data from Caucasians were included and the source was identified to ensure that none were duplicated in the analyses. For each isoform, abundance values were tested for homogeneity and shape of the distribution. Following calculation of the weighted mean, standard deviation and coefficient of variation (CV) [3], the geometric mean (GM) and the geometric standard deviation were derived assuming a log-normal distribution [4].

Abundances derived for each of the isoforms in this study and those reported by Shimada et al. [2] are shown in the table. With the exception of CYP1A2 and CYP2D6, mean values from the meta-analysis appear to be greater. The values reported in our study are based on 42 to 241 liver samples and therefore may give a more realistic representation of CYP abundance and its variability in the Caucasian population than those reported [2] and cited frequently by many research groups. In view of the possible differences between Japanese and Caucasians [2] a meta-analysis similar to the one presented here is warranted to derive abundance values for the Japanese population and possibly other ethnic groups.

Table Abundance of CYPs (pmol P450 mg^{-1} protein) in human liver determined from a meta-analysis of all reported data and those cited by Shimada et al (1994).

	Meta-analysis			**Shimada**					
				All (n=60)			**Caucasian (n=30)**		
	Mean	**GM**	**CV**	**Mean**	**GM**	**CV**	**Mean**	**GM**	**CV**
1A2	52	37	67	42	37	55	58	53	47
2A6	36	29	84	14	10	93	23	19	73
2B6	11	7	147	1	1	200	2	1	86
2C	-	-	-	60	55	45	77	72	35
2C8	24	19	81	-	-	-	-	-	-
2C9	73	60	54	-	-	-	-	-	-
2C19	14	9	106	-	-	-	-	-	-
2D6	8	7	61	5	4	80	9	7	62
2E1	61	49	61	22	19	55	27	24	46
3A	155	131	67	96	85	53	120	114	35

No of livers used in the meta-analysis was 119 (1A2), 42 (2A6), 241 (2B6), 114 (2C8), 174 (2C9), 126 (2C19), 98 (2D6), 234 (2E1) and 219 (3A). Data for Caucasian samples were derived from data in Shimada et al. (1994).

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2. Shimada T., *et al. J Pharmacol Exp Ther* 1994; 270: 414-423.
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4. Aitchison and Brown (1996) *The log-normal distribution*, University Press, Cambridge.