

Supplemental Table 1. Minor allele frequencies of CYP2C9 *2, *3, *8, and *9 in different populations.

CYP2C9 Variant	Genetic Impact	Minor Allele Frequency (MAF)			
		European	African	Eastern Asian	South Asian
*2	Arg144Cys	0.13 ^a	0.02	< 0.01	0.05
*3	Ile359Leu	0.07	0.01	0.03	0.11
*8	Arg150His	< 0.01	0.06	< 0.01	< 0.01
*9	His251Arg	< 0.01	0.08	< 0.01	< 0.01

^a MAF > 0.02 are bolded.

Supplemental Table 2. Impact of CYP2C9 *2, *3, *8, and *9 variants on Δ 8-THC 11'-hydroxylation.

Rec CYP2C9 microsomes ^b	Amino acid change	Fold-difference as compared to CYP2C9*1 ^a		
		$K_{m,u}$ or $S_{50,u}$ (μ M) ^c	V_{max} (pmol·min ⁻¹ ·mg ⁻¹ protein)	CL_{int} or CL_{max} (μ L·min ⁻¹ ·mg ⁻¹ protein)
*2	Arg144Cys	27 (0.028)	1.3 (0.0527)	34 (0.010)
*3	Ile359Leu	58 (0.0032)	1.0 (0.78)	58 (0.0099)
*8	Arg150His	246 (0.051)	11 (0.032)	21 (0.011)
*9	His251Arg	16 (0.0091)	2.2 (0.0059)	58 (0.0099)

^a Comparisons were assessed using a two-sided Student's t-test, with all tests considered statistically significant at $P < 0.05$ (bolded). Values in parenthesis are the P-values vs CYP2C9*1.

^b Rec, microsomes from recombinant P450 overexpressing HEK293 cells.

^c S_{50} is the substrate concentration resulting in 50% of V_{max} (analogous to K_m in the Michaelis-Menten model). $K_{m,u}$ or $S_{50,u}$ is the corrected K_m or S_{50} by multiplying the unbound fraction (f_u) of Δ 9-THC in the tube (0.051 in HLM, and 0.043 in recombinant P450 microsomes).