

**Table 1** Human studies with pharmacokinetic data considered for analysis

References	Route of administration	Dose	Measured biomarkers	Number of subjects (sex)	Use in model development: training (T) or test/validation (V)
Ameer et al. (1981)	Oral	650 mg	Plasma: APAP	1 (M)	V
	IV	650 mg	Plasma: APAP	1 (M)	V
Chen et al. (1996)	Oral	1,000 mg	Plasma and urine: APAP, APAP-G, APAP-S	10 (M/F)	<sup>a</sup>
Chiew et al. (2010)	Oral	80 mg/kg	Plasma: APAP, APAP-G, APAP-S	9 (M/F)	T
Chan et al. (1997)	Oral	20 mg/kg	Plasma: APAP, APAP-G, APAP-S	6 (M/F)	T
Critchley et al. (2005)	Oral	20 mg/kg	Plasma and urine: APAP, APAP-G, APAP-S	11 (M/F)	V
	Oral	20 mg/kg	Plasma and urine: APAP, APAP-G, APAP-S	9 (M/F)	V
Critchley et al. (1986)	Oral	1,500 mg	Urine: APAP, APAP-G, APAP-S	111 (M/F)	T
Esteban et al. (1996)	Oral	1,500 mg	Urine: APAP, APAP-G, APAP-S	71 (M/F)	V
Jensen et al. (2004)	Oral	1,000 mg	Plasma: APAP, APAP-G, APAP-S	6 (M/F)	V
Itoh et al. (2001)	Oral	1,000 mg	Plasma: APAP, APAP-G, APAP-S	5 (M)	V
Kamali (1993)	Oral	1,500 mg	Plasma: APAP, urine: APAP, APAP-G, APAP-S	10 (M/F)	V
Kim et al. (2011)	Oral	1,000 mg	Plasma: APAP, APAP-G, APAP-S	12 (M/F)	V
Lau and Critchley (1994)	Oral	20 mg/kg	Plasma and urine: APAP, APAP-G, APAP-S	6 (M/F)	T
Prescott (1980)	Oral	20 mg/kg	Plasma and urine: APAP, APAP-G, APAP-S	8 (M/F)	T
	Oral	12 mg/kg	Plasma: APAP	4 (M/F)	T
	IV	12 mg/kg	Plasma: APAP	4 (M/F)	T
Prescott (1989)	Oral	1,000 mg	Plasma: APAP, APAP-G, APAP-S	10	V
Rawlins and Henderson (1977)	Oral	500 mg	Plasma: APAP	6 (M)	V
	Oral	1,000 mg	Plasma: APAP	6 (M)	V
	Oral	2,000 mg	Plasma: APAP	6 (M)	V
	IV	1,000 mg	Plasma: APAP	6 (M)	T
Shinoda et al. (2077)	Oral	1,000 mg	Plasma: APAP, APAP-G, APAP-S	5 (M/F)	T
Tan et al. (2012)	Oral	500 mg	Plasma and urine: APAP, APAP-G	12 (°)	T
Tonoli et al. (2012)	IV	1,000 mg	Plasma: APAP, APAP-G	2 (°)	V
Volak et al. (2013)	Oral	325 mg	Plasma: APAP, APAP-G, APAP-S	8 (M/F)	T
Yin and Tomlinson (2001)	Oral	500	Plasma: APAP	12 (M)	V
Zhu et al. (2007)	Oral	650 mg	Plasma: APAP	10 (M)	<sup>b</sup>

<sup>a</sup> Data were not used. APAP-G measurement methodology was different from that used in other studies

<sup>b</sup> Data were not used. APAP was administered in combination with Tramadol

<sup>c</sup> Not specified