

Supplementary Information to the manuscript by Fairman et al.

Table S1. Reporting a list of chemicals for which a PBPK model is available, reporting are the administration route, model compartments Simulation software used and reference/DOI. The information was extracted from the Thompson (2021, DOI: 10.1177/02611929211060264) database on PBPK models.

Chemical Name	Sex/ Life stage	Administration Route	Compartments or related information	Simulation Software	Reference	DOI
alfentanil	From birth	Intravenous infusion		Simcyp	Abduljalil et al, 2019, Clin Pharmacokinet, 59, 501-518	10.1007/s40262-019-00827-4
alfentanil		Intravenous bolus injection	adipose, brain, caecum, colon, duodenum, gut, heart, kidney, liver, lung, jejunum, ileum, marrow, muscle, reproductive organs, rest of body, skin, spleen	GastroPlus	Baneyx et al., 2014, Eur J Pharm Sci, 56, 1-15	10.1016/j.ejps.2014.02.002
alfentanil		Oral bolus	adipose, brain, caecum, colon, duodenum, gut, heart, kidney, liver, lung, jejunum, ileum, marrow, muscle, reproductive organs, rest of body, skin, spleen	GastroPlus	Baneyx et al., 2014, Eur J Pharm Sci, 56, 1-15	10.1016/j.ejps.2014.02.002

buprenorphine		Intravenous bolus injection	lung, adipose, bone, brain, heart, kidney, muscle, liver, portal vein, pancreas, spleen, gut, venous, arterial	Simcyp	Kalluri et al, 2017, Br J Clin Pharmacol, 83, 2458-2473	10.1111/bc p.13368
buprenorphine		Buccal	lung, adipose, bone, brain, heart, kidney, muscle, liver, portal vein, pancreas, spleen, gut, venous, arterial	Simcyp	Kalluri et al, 2017, Br J Clin Pharmacol, 83, 2458-2473	10.1111/bc p.13368
buprenorphine		Dermal injection	central compartment, periphery	Simcyp	Liu and Gobburu, 2018, J Pharm Sci, 107, 942-948	10.1016/j.x phs.2017.1 0.035
buprenorphine		Intravenous bolus injection	central compartment, periphery	Simcyp	Liu and Gobburu, 2018, J Pharm Sci, 107, 942-948	10.1016/j.x phs.2017.1 0.035
carfentanil	Male/adult	iv-administered		GastroPlus	Feasel et al. 2018	https://apps.dtic.mil/sti/pdfs/AD1060142.pdf
cocaine	Male	Intravenous bolus injection	lung, brain, fat, bone, heart, muscle, kidney, skin, spleen, intestine, liver, venous, arterial	MATLAB	Bravo-Gómez et al, 2019, Toxicol Res (Camb), 8, 432-446	10.1039/c8 tx00309b
cocaine	Adult (typical)	Intravenous bolus injection		GastroPlus	Cheng et al, 2019, ACS Chem	10.1021/ac schemneu

					Neurosci, 10, 3486-3499	ro.9b00109
ethanol		Inhalation	lung, fat, liver, brain, well/rapidly perfused, poorly/slowly perfused	acsIX	Crowell et al., 2015, Regul Toxicol Pharmacol, 73, 452-62	10.1016/j.yrtph.2015.07.021
ethanol		Metabolism from parent	lung, fat, liver, brain, well/rapidly perfused, poorly/slowly perfused	acsIX	Crowell et al., 2015, Regul Toxicol Pharmacol, 73, 452-62	10.1016/j.yrtph.2015.07.021
ethanol		Inhalation	bone marrow, fat, gastrointestinal tract, kidney, liver, lung, poorly/slowly perfused, well/rapidly perfused		Dennison, Bigelow and Andersen, 2004, Toxicol Ind Health, 20, 165-75	10.1191/0748233704th203oa
ethanol		Oral bolus	bone marrow, fat, gastrointestinal tract, kidney, liver, lung, poorly/slowly perfused, well/rapidly perfused		Dennison, Bigelow and Andersen, 2004, Toxicol Ind Health, 20, 165-75	10.1191/0748233704th203oa
ethanol	Male/Adult	Inhalation	brain, fat, liver, lung, poorly/slowly perfused, well/rapidly perfused	acsIX	Dumas-Campagna et al., 2014, Inhal Toxicol, 26, 59-69	10.3109/08958378.2013.853714

ethanol	Female/adult	Inhalation	brain, fat, liver, lung, poorly/slowly perfused, well/rapidly perfused	acsIX	Dumas-Campagna et al., 2014, Inhal Toxicol, 26, 59-69	10.3109/08958378.2013.853714
Ethanol		Intravenous bolus injection		PKQuest	Levitt, 2002, BMC Clin Pharmacol, 2, 4	10.1186/1472-6904-2-4
ethanol		Oral bolus		PKQuest	Levitt, 2002, BMC Clin Pharmacol, 2, 4	10.1186/1472-6904-2-4
ethanol		Oral bolus	gut, liver, lung, muscle, stomach, well/rapidly perfused, poorly/slowly perfused	MATLAB	MacDonald et al, 2002, Regul Toxicol Pharmacol, 35, 165-76	10.1006/rtph.2001.1507
ethanol	Male/From birth	Inhalation	brain, fat, liver, lung, poorly/slowly perfused, well/rapidly perfused	Multiple software used	Pastino et al., 1997, Toxicol Appl Pharmacol, 145, 147-57	10.1006/taap.1997.8161
ethanol	Male/From birth	Intravenous infusion	brain, fat, liver, lung, poorly/slowly perfused, well/rapidly perfused	Multiple software used	Pastino et al., 1997, Toxicol Appl Pharmacol, 145, 147-57	10.1006/taap.1997.8161
ethanol	Male (Caucasian)	Inhalation	brain, fat, gastrointestinal tract, liver, lung, poorly/slowly		Pastino, Flynn and Sultatos, 2000, Drug Chem Toxicol, 23, 179-201	10.1081/dct-100100110

			perfused, well/rapidly perfused			
ethanol	Male (African American)	Inhalation	brain, fat, gastrointestinal tract, liver, lung, poorly/slowly perfused, well/rapidly perfused		Pastino, Flynn and Sultatos, 2000, Drug Chem Toxicol, 23, 179-201	10.1081/dc t- 100100110
ethanol	Male (Caucasian)	Oral bolus	brain, fat, gastrointestinal tract, liver, lung, poorly/slowly perfused, well/rapidly perfused		Pastino, Flynn and Sultatos, 2000, Drug Chem Toxicol, 23, 179-201	10.1081/dc t- 100100110
ethanol	Male (African American)	Oral bolus	brain, fat, gastrointestinal tract, liver, lung, poorly/slowly perfused, well/rapidly perfused		Pastino, Flynn and Sultatos, 2000, Drug Chem Toxicol, 23, 179-201	10.1081/dc t- 100100110
ethanol		Inhalation			Plawecki et al., 2007, Biomed Signal Process Control, 2, 97-110	10.1016/j.b spc.2007.0 4.001
ethanol	Male/Adult	Intravenous infusion			Ramchandani et al., 2009, Alcohol Clin Exp Res, 33, 938-44	10.1111/j.1 530-

						0277.2009.00906.x
ethanol	Female/adult	Intravenous infusion			Ramchandani et al., 2009, Alcohol Clin Exp Res, 33, 938-44	10.1111/j.1530-0277.2009.00906.x
fentanyl		Intravenous infusion	arterial, brain, carcass, fat, gut, heart, kidney, liver, lung, muscle, pancreas, skin, spleen, venous	MATLAB	Björkman, 2003, J Pharmacokinet Pharmacodyn, 30, 285-307	10.1023/a:1026194618660
fentanyl	Adult (typical)	Intravenous bolus injection		GastroPlus	Cheng et al, 2019, ACS Chem Neurosci, 10, 3486-3499	10.1021/acscchemneuro.9b00109
fentanyl		Intravenous bolus injection		MATLAB	Huang and Isoherranen, 2019, J Pharmacol Exp Ther, 372, 30-45	10.1124/jpet.119.262154
fentanyl		Buccal		MATLAB	Huang and Isoherranen, 2019, J Pharmacol Exp Ther, 372, 30-45	10.1124/jpet.119.262154
methadone	Female/pregnant	Oral bolus		Multiple software used	Ke et al., 2014, Br J Clin Pharmacol, 77, 554-70	10.1111/bcp.12207
methadone		Intravenous bolus injection	adipose, bone, brain, gastrointestinal tract, heart, kidney, liver, lung, marrow,	MATLAB	Yang et al., 2006, J Pharmacokinet Pharmacodyn, 33, 485-518	10.1007/s10928-006-9018-0

			muscle, pancreas, skin, spleen, thyroid			
methadone		Oral bolus	adipose, bone, brain, gastrointestinal tract, heart, kidney, liver, lung, marrow, muscle, pancreas, skin, spleen, thyroid	MATLAB	Yang et al., 2006, J Pharmacokinet Pharmacodyn, 33, 485-518	10.1007/s1 0928-006- 9018-0
morphine	Adult (typical)	Intravenous bolus injection		Simcyp	Emoto et al, 2017, CPT Pharmacometrics Syst Pharmaacol, 6, 110-119	10.1002/ps p4.12144
morphine	From birth	Intravenous bolus injection		Simcyp	Emoto et al, 2017, CPT Pharmacometrics Syst Pharmaacol, 6, 110-119	10.1002/ps p4.12144
morphine	From birth	Intravenous bolus injection		Simcyp	Emoto et al, 2018, CPT Pharmacometrics Syst Pharmacol, 7, 464-473	10.1002/ps p4.12306
morphine		Intravenous bolus injection	lung, brain, muscle, adipose, marrow, intestine, spleen, liver, kidney, arterial, venous		German, Pilvankar and Przekwas, 2019, J Pharmacokinet Pharmacodyn, 46, 513-529	10.1007/s1 0928-019- 09648-1
morphine		Intravenous infusion	lung, brain, muscle, adipose, marrow, intestine, spleen,		German, Pilvankar and Przekwas, 2019, J Pharmacokinet	10.1007/s1 0928-019- 09648-1

			liver, kidney, arterial, venous		Pharmacodyn, 46, 513-529	
morphine		Intravenous bolus injection	liver	Simcyp	Prasad et al., 2018, Drug Metab Dispos, 46, 943-952	10.1124/dmd.118.080523
morphine	From birth	Intravenous bolus injection	liver	Simcyp	Prasad et al., 2018, Drug Metab Dispos, 46, 943-952	10.1124/dmd.118.080523
morphine	Male/Adult	Intravenous bolus injection		PK-Sim/MoBi	Schlender et al, 2016, Clin Pharmacokinet, 55, 1573-1589	10.1007/s40262-016-0422-3
morphine	Female/adult	Intravenous bolus injection		PK-Sim/MoBi	Schlender et al, 2016, Clin Pharmacokinet, 55, 1573-1589	10.1007/s40262-016-0422-3
morphine	Male/old age	Intravenous bolus injection		PK-Sim/MoBi	Schlender et al, 2016, Clin Pharmacokinet, 55, 1573-1589	10.1007/s40262-016-0422-3
morphine	Female/old age	Intravenous bolus injection		PK-Sim/MoBi	Schlender et al, 2016, Clin Pharmacokinet, 55, 1573-1589	10.1007/s40262-016-0422-3
morphine	From birth	Intravenous infusion		PK-Sim/MoBi	Strougo et al., 2012, J Pharmacokinet Pharmacodyn, 39, 195-203	10.1007/s10928-012-9241-9
morphine	Adult (typical)	Intravenous infusion	plasma, brain	NONMEM	Yamamoto et al, 2018, Eur J Pharm Sci, 112, 168-179	10.1016/j.ejps.2017.11.011
N,O-didesmethyltramadol	Adult (typical)	Intravenous bolus injection		Simcyp	T'jollyn et al., 2015, Pharm Res, 32, 260-74	10.1007/s11095-014-1460-x

N-desmethyltramadol	Adult (typical)	Metabolism from parent		Simcyp	T'jollyn et al., 2015, Pharm Res, 32, 260-74	10.1007/s1095-014-1460-x
O-desmethyltramadol	Adult (typical)	Metabolism from parent		Simcyp	T'jollyn et al., 2015, Pharm Res, 32, 260-74	10.1007/s1095-014-1460-x
oxycodone	Adult (typical)	Intravenous infusion	plasma, brain	NONMEM	Yamamoto et al, 2018, Eur J Pharm Sci, 112, 168-179	10.1016/j.ejps.2017.11.011
oxycodone	From birth	Intravenous bolus injection		PK-Sim/MoBi	Zheng et al., 2019, Pharm Res, 36, 171	10.1007/s1095-019-2708-2
oxycodone	From birth	Oral bolus		PK-Sim/MoBi	Zheng et al., 2019, Pharm Res, 36, 171	10.1007/s1095-019-2708-2
oxycodone	Male/Adult	Intravenous bolus injection		PK-Sim/MoBi	Zheng et al., 2019, Pharm Res, 36, 171	10.1007/s1095-019-2708-2
oxycodone	Male/Adult	Oral bolus		PK-Sim/MoBi	Zheng et al., 2019, Pharm Res, 36, 171	10.1007/s1095-019-2708-2
remifentanyl		Intravenous infusion	plasma, tissue, gastrointestinal tract small intestine, large intestine, gall bladder, liver, poorly/slowly perfused, well/rapidly perfused		Abbiati and Manca, 2017, Curr Drug Deliv, 14, 190-202	10.2174/1567201813666160524142031

remifentanil		Intravenous infusion	large intestine, small intestine, stomach, liver, plasma, poorly/slowly perfused, well/rapidly perfused	MATLAB	Cascone et al, 2018, Eur J Phar Sci, 111, 20-28	10.1016/j.ejps.2017.09.028
remifentanil		Intravenous bolus injection	large intestine, small intestine, stomach, liver, plasma, poorly/slowly perfused, well/rapidly perfused	MATLAB	Cascone et al, 2018, Eur J Phar Sci, 111, 20-28	10.1016/j.ejps.2017.09.028
R-methadone	Female/pregnant	Oral bolus		Multiple software used	Ke et al., 2014, Br J Clin Pharmacol, 77, 554-70	10.1111/bcp.12207
S-methadone	Female/pregnant	Oral bolus		Multiple software used	Ke et al., 2014, Br J Clin Pharmacol, 77, 554-70	10.1111/bcp.12207
sufentanil	Children	Intravenous bolus injection		SimCyp	Zhou et al., 2018	https://doi.org/10.1002/cpt.904
sufentanil	Adult (typical)	Intravenous bolus injection		SimCyp	Zhou et al., 2018	https://doi.org/10.1002/cpt.905
tramadol	Adult (typical)	Intravenous bolus injection		Simcyp	T'Jollyn et al, 2015, AAPS J, 17, 1376-87	10.1208/s12248-015-9803-z

tramadol	Adult (typical)	Intravenous bolus injection		Simcyp	Tjollyn et al., 2015, Pharm Res, 32, 260- 74	10.1007/s1 1095-014- 1460-x
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