Drug Metabolism and Disposition

Deciding on Success Criteria for Predictability of Pharmacokinetic Parameters from In Vitro Studies: An Analysis Based on In Vivo Observations

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Supplemental Table A. Collected clinical data for CL and V_{ss} after intravenous administration for 17 different compounds

Compound	Systemic Clearance (CLiv)				Volume of distribution (Vss)			
	No. of Trials	Total no. of Subjects	Mean %CV (range)	References	No. of Trials	Total no. of Subjects	Mean %CV (range)	References
Talinolol	7	72	16 (11 – 26)	[1-7]	NA	NA	NA	NA
Propranolol	12	102	17 (3 – 41)	[8-15]	NA	NA	NA	NA
Cisatracurium	12	210	18 (3 – 32)	[16-25]	NA	NA	NA	NA
Acetaminophen	11	146	19 (7 – 31)	[26-35]	12	146	19 (11 – 27)	[26-35]
Lidocaine	11	104	20 (6 – 32)	[36-45]	9	90	21 (9 – 28)	[36-40, 43-46]
Propofol	15	305	21 (5 – 60)	[47-58]	NA	NA	NA	NA
Metronidazole	17	182	21 (6 – 43)	[59-70]	12	184	24 (7 – 50)	[59, 61-71]
Theophylline	21	230	22 (6 – 83)	[72-91]	NA	NA	NA	NA
Ciprofloxacin	18	265	23 (10 – 60)	[92-109]	15	190	21 (13 – 39)	[92, 94-97, 99, 100, 102, 104, 107-109]
Midazolam	33	570	23 (6 – 46)	[110-142]	21	251	17 (2 – 40)	[110, 112, 116-120, 122, 124-126, 129, 132-138, 140]
Antipyrine	10	257	23 (6 – 48)	[27, 30, 32, 34, 143-147]	10	297	14 (4 – 33)	[27, 30, 32, 34, 143, 145-148]
Digoxin	18	202	25 (13-47)	[149-165]	8	110	32 (11 – 64)	[149, 150, 153-157, 159]
Furosemide	15	99	25 (7 – 50)	[166-180]	11	72	22 (6 – 58)	[166, 167, 169, 172, 174, 179, 181-185]
Thiopental	18	180	29 (11 – 56)	[186-202]	12	117	37 (14 – 73)	[186-191, 195-198, 200, 201]
Lorazepam	21	196	30 (10-49)	[26, 27, 89, 131, 143, 144, 203-214]	15	136	18 (8 – 34)	[26, 27, 30, 131, 143, 205, 206, 208, 209, 211, 212, 215-218]
Diazepam	21	301	31 (11 – 51)	[27, 127, 131, 143, 206, 211, 219-232]	14	152	32 (11 – 57)	[26, 27, 143, 206, 211, 219, 221, 223-226, 229, 230]
Alfentanil	14	193	40 (7 – 68)	[122, 123, 233-243]	NA	NA	NA	NA

NA= not applicable (data was not available).

Supplemental Table B. Percentage of 100,000 simulated trial means outside two-fold limits stratified by sample size and CV% (σ)

CV(%)	Trial size															
	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
10	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
20	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
30	0.21	0.062	0.022	0.012	0.003	0.002	0	0	0	0	0	0	0	0	0	0
40	1.868	0.959	0.543	0.306	0.169	0.091	0.037	0.025	0.009	0.006	0.006	0.001	0.001	0	0.001	0
50	5.543	3.533	2.384	1.526	1.016	0.659	0.449	0.32	0.223	0.121	0.121	0.071	0.035	0.029	0.024	0.019
60	10.052	7.225	5.314	3.908	2.837	2.099	1.487	1.152	0.846	0.607	0.607	0.35	0.269	0.174	0.155	0.113
70	14.951	11.67	8.992	6.913	5.452	4.158	3.377	2.533	1.981	1.613	1.613	1.008	0.818	0.674	0.514	0.39
80	19.765	15.95	12.944	10.434	8.335	6.776	5.605	4.585	3.765	3.125	3.125	2.119	1.673	1.449	1.214	1.013
90	23.899	19.901	16.379	13.746	11.307	9.496	7.988	6.763	5.699	4.969	4.969	3.497	2.964	2.553	2.139	1.91
100	27.584	23.295	19.942	16.942	14.155	12.313	10.716	9.184	7.914	6.911	6.911	5.052	4.388	3.952	3.397	2.916
110	30.886	26.765	23.081	19.721	17.068	15.013	13.151	11.738	10.073	8.648	8.648	6.798	5.99	5.27	4.764	4.269
120	33.591	29.329	25.629	22.494	19.925	17.397	15.465	13.752	11.929	10.68	10.68	8.538	7.534	6.93	6.174	5.578
130	36.366	31.462	27.925	24.866	22.076	19.685	17.685	15.575	14.163	12.52	12.52	10.283	9.247	8.335	7.514	6.706
140	38.383	34.028	30.229	27.011	24.107	22.027	19.793	17.736	16.257	14.412	14.412	12.08	10.942	9.99	8.988	8.082
150	40.764	35.95	32.311	29.115	26.095	23.704	21.477	19.715	17.713	16.203	16.203	13.623	12.28	11.208	10.322	9.44

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