

Table A.1. Compound list for all macro-molecule drugs

	Compounds	MW (kDa)	Observed CL (Mean (CV%), ml/hr/kg) in		Reference	Group
			human	a		
1	Abciximab	47.6	288 (59)		(Abernethy et al., 2002)	1
2	Alefacept	51.8	0.25		(Tang et al., 2004)	
3	Alteplase ^a	67.5	894 (14)	34.8	0.863	(Martin et al., 1991, Martin et al., 1992)
4	ANF ^a	67.5	2229 (11)	112	0.847	(Yandle et al., 1986, Cernacek et al., 1988, Krieter and Trapani, 1989, Marleau et al., 1989)
5	BM06.022 ^a	39.0	239 (13)	6.98	0.893	(Martin et al., 1991)
6	Cetrorelix	1.49	72			(Obach et al., 2008)
7	Cyclosporin ^a	1.20	321 (38)	5.51	1.15	(Sangalli et al., 1988)
8	Dalbavancin	1.82	0.61 (3.6)			(Obach et al., 2008)
9	Daptomycin	1.62	9.0 (10)			(Obach et al., 2008)
10	Darbepoetin alfa	37.1	2.3 (35)			(Egrie Jc Fau - Dwyer et al., 2003)
11	Denileukin diftitox	57.6	105 (20)			(Tang et al., 2004)
12	Desmopressin	1.07	143 (34)			(Agero H Fau - Seiding Larsen et al.) (Grene-Lerouge Na Fau - Bazin-Redureau et al., 1996, Ujhelyi and Robert, 1995)
13	Digoxin-Fab ^a	45.5	19 (32)	1.017	0.667	(Olsen and Martin, 2002)
14	Drotrecogin- α	55.0	314 (31)			(Halstenson et al., 1991)
15	EPO- α	30.4	8.1 (12)			(Bleuel et al., 1996, Halstenson et al., 1991)
16	EPO- β ^a	36.0	7.9 (15)	0.234	0.660	(Keith et al., 1995, McCarthy et al., 2002, White et al., 1998)
17	Factor IX ^a	56.5	9.1 (16)	0.288	0.715	(Tang et al., 2004)
18	Filgrastim	18.8	36 (24)			(Gatti et al., 1991)
19	GLQ223 ^b	27.0	130 (54)			(Tang et al., 2004)
20	Glucagon	3.50	810			(Kagan et al., 2010)
21	IFN β 1a ^a	22.5	573 (47)	4.98	0.907	(Kagan et al., 2010)
22	IFN β 1b ^b	18.5	760 (37)			(Geary et al., 2001)
23	ISIS 2503 ^a	NA	144	2.41	0.879	

24	ISIS 3521 ^a	6.72	67 (2.7)	2.12	0.599	(Geary et al., 2001)
25	ISIS 5132 ^a	6.63	76 (32)	3.23	0.873	(Geary et al., 2001)
26	ISIS 104838 ^a	7.41	41 (12)	155	0.709	(Sewell et al., 2002, Geary et al., 2003)
27	ISIS 301012 ^b	7.39	41 (12)	96.8	0.487	(Yu et al., 2007)
28	Leuprolide	1.21	114 (7.4)			(Obach et al., 2008)
29	Nartograstim ^a	19	29 (11)	49.2	0.655	(Kuwabara et al., 1994, Ohdo et al., 1998)
30	Octreotide	1.00	121 (25)			(Tang et al., 2004)
31	Pamiteplase ^a	37.0	130 (7.7)	2.06	0.913	(Oikawa et al., 2000, Oikawa et al., 2001)
32	PEG-EPO ^a	60.0	0.50 (6.0)	1.95	0.674	(Macdougall et al., 2006)
33	PEG-IL2 ^a	22.0	6.0	0.179	0.750	(Braeckman, 2000)
34	rCD4 ^a	50.0	49 (43)	3.36	0.577	(Mordenti et al., 1991)
35	Relaxin ^a	6.00	139 (37)	5.83	0.776	(Mordenti et al., 1991)
36	rEPO ^a	36.0	10.1 (35)	0.221	0.921	(Flaharty et al., 1990, Woo and Jusko, 2007)
37	Reteplase ^a	39.6	300 (40)			(Tang et al., 2004)
38	rhGH ^a	20.0	124	6.47	0.688	(Mordenti et al., 1991)
39	rhIL-2 ^a	15.0	165 (54)	4.79	0.650	(Braeckman, 2000)
40	rHirudin ^a	6.91	168	8.48	1.01	(Nowak, 1991)
41	rHuIFN- α A ^a	19.0	169 (38)	3.68	0.710	(Lave et al., 1995)
42	rHuIL-10	18.0	65 (11)			(Radwanski et al., 1998)
43	rt-PA ^a	63.0	490	16.2	0.862	(Mordenti et al., 1991, Collen et al., 1991)
44	SK&F 107647	1.17	65 (28)			(Brocks et al., 1996)
45	SR 90107A ^a	1.11	6.3 (16)	41.2	0.506	(Herault et al., 1997)
46	Teicoplanin A2-1	1.88	12 (5.0)			(Obach et al., 2008)
47	Telavancin	1.76	12 (12)			(Obach et al., 2008)
48	Tenecteplase ^a	59.0	83 (14)	3.35	0.903	(Tanswell et al., 2002)
49	Valspodar	1.22	156			(Obach et al., 2008)
50	Vancomycin	1.45	112 (5.4)			(Obach et al., 2008)
51	Abatacept ^a	92.0	0.23	0.563	0.647	(Srinivas et al., 1997, Srinivas et al., 1996a, Srinivas et al., 1996b)

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52	Adalimumab ^b	148	0.13 (31)			(Lobo et al., 2004, Weisman et al., 2003)
53	Basiliximab	144	0.59 (46)			(Tang et al., 2004)
54	Bevacizumab ^a	149	0.12 (42)	0.0046	0.684	(Lin et al., 1999, Gordon et al., 2001)
55	CD4-IgG ^a	98.0	1.9	0.102	0.740	(Mordenti et al., 1991)
56	Cetuximab ^b	146	0.50 (37)			(Lobo et al., 2004)
57	CNTO136 ^b	NA	0.19 (32)			(Ling et al., 2009)
58	CNTO328 ^b	145	0.47 (34)			(Ling et al., 2009, Puchalski et al.)
59	CNTO95 ^b	180	0.28 (13)			(Ling et al., 2009, Mullamitha et al., 2007)
60	Daclizumab ^b	143	0.19			(Tang et al., 2004, Ling et al., 2009)
61	Eculizumab	148	0.29 (12)			#
62	Efalizumab ^b	150	0.65 (32)			(Ling et al., 2009, Bauer et al., 1999)
63	EGFr3 ^a	150	0.98 (18)	0.0865	1.02	(Crombet et al., 2001)
64	Factor VIII ^a	340	3.0	0.182	0.744	(Mordenti et al., 1996, Stokol et al., 1997)
65	Gemtuzumab	152	3.3 (85)			(Dowell et al., 2001)
66	Golimumab ^b	147	0.28 (79)			(Ling et al., 2009)
67	Horse F(ab')2 ^a	100	0.93 (84)	0.0328	0.534	(Bazin-Redureau et al., 1998, Ho et al., 1990) (Tang et al., 2004, Palframan R Fau - Airey et al., 2009, Rojas et al., 2005)
68	Infliximab ^a	144	0.14 (20)	0.0075	0.540	(Tang et al., 2004)
69	Laronidase	83.0	132 (32)			(Tang et al., 2004)
70	Lenercept ^a	120	0.30	0.008	1.06	(Richter Wf Fau - Gallati et al., 1999)
71	Natalizumab ^b	149	0.27 (1.5)			(Ling et al., 2009, Sheremata et al., 1999)
72	Panitumumab ^b	147	0.20 (10)			(Ling et al., 2009, Cohenuram and Saif, 2007)
73	Pertuzumab ^a	150	0.14 (36)	0.259	0.926	(Agus et al., 2005, Adams et al., 2006)
74	Rituximab	145	0.13			(Cartron et al., 2007)
75	RSHZ19 ^a	146	0.122 (15)	0.0035	0.731	(Davis et al., 1995, Everitt et al., 1996)
76	Tanezumab ^b	145	0.11			#
77	Tositumomab	144	0.97			(Lobo et al., 2004)
78	Trastuzumab ^b	146	0.41 (61)			(Tang et al., 2004, Ling et al., 2009)
79	Ustekinumab ^b	146	0.093 (28)			(Ling et al., 2009)

a. PK data available in ≥ 3 animal species and in human

b. PK data available in monkey and human

Eculizumab; http://www.accessdata.fda.gov/drugsatfda_docs/nda/2007/125166s0000_PharmacometricsR.pdf

Tanezumab; http://www.aapsj.org/abstracts/NBC_2009/NBC09-000419.PDF

Table A.2. Compound list of small molecule drugs used for interspecies scaling

	Compounds	MW	Observed CL	Character	Elimination	Fu%	a	b	Reference
			(Mean (CV%), ml/min/kg) in human						
1	Acivicin	178.6	0.78 (27)	Acid	Mixed	100	4.10	0.558	(Mahmood and Balian, 1996)
2	Actisomide	369.6	6.8 (16)	Base	Mixed	NA	10.9	1.04	(Mahmood and Balian, 1996)
3	Amethopterin	454.4	3.5	Acid	Renal	50	10.4	0.724	(Dedrick et al., 1970)
4	Amiodarone	645.3	1.9	Base	Hepatic	4.4	13.5	0.979	(Evans et al., 2006)
5	Amphotericin B	924.1	0.34 (75)	Zwitt	Hepatic	5.2	0.967	0.847	(Hutchaleelaha et al., 1997, Robbie and Chiou, 1998)
6	Antipyrine	188.2	0.78 (21)	Base	Hepatic	100	11.7	0.843	(Lave et al., 1997)
7	Ara-C	243.2	1.3	Base	Hepatic	98	4.21	0.830	(Dedrick et al., 1973)
8	Betamipron	193.2	6.6 (12)	Acid	Renal	48	13.7	0.782	(Mahmood, 1998)
9	Biperiden	311.5	15	Base	Hepatic	40	44.6	0.719	(Evans et al., 2006)
10	Bosentan	569.6	1.9 (26)	Acid	Hepatic	2	24.9	0.562	(Lave et al., 1997)
11	Caffeine	194.2	2.0 (11)	Neutral	Hepatic	96	8.07	0.584	(Lave et al., 1997)
12	Cefmetazole	471.5	1.7 (26)	Base	Renal	15	12.8	0.633	(Feng et al., 2000)
13	Cefotetan	619.6	0.60 (15)	Acid	Renal	12	7.15	0.641	(Mahmood and Balian, 1996)
14	Cefazolin	454.5	0.88	Base	Renal	13	4.79	0.733	(Mahmood and Balian, 1996)
15	Cefodizime	584.7	0.74 (24)	Acid	Renal	12	1.51	1.00	(Matsushita et al., 1990)
16	Cefoperazone	645.7	1.4 (14)	Base	Hepatic	18	6.75	0.578	(Lave et al., 1997)
17	Cefpiramide	612.6	0.48 (42)	Base	Renal	3.7	4.27	0.443	(Nakagawa et al., 1984)
18	Ceftizoxime	405.4	2.4 (21)	Base	Renal	72	10.3	0.544	(Mahmood and Balian, 1996)
19	Chlorpromazine	318.9	4.3	Base	Hepatic	10	47.1	0.889	(Evans et al., 2006)
20	CI-1007	329.5	21	Base	Hepatic	2	35.0	0.905	(Feng et al., 1998)
21	Ciprofloxacin	331.4	6.0	Acid	Renal	60	14.5	0.939	(Siefert et al., 1986, Nouws et al., 1988)
22	Coumarin	206.2	16 (24)	Acid	Hepatic	14	21.2	1.10	(Ritschel et al., 1991)
23	Cytosin	279.1	2.25 (79)	Acid	Hepatic	100	21.0	0.843	(Mellett, 1969)
24	DA-1131	445.6	5.0	Acid	Mixed	90	11.6	0.825	(Kim et al., 1998)
25	Diazepam	284.8	0.32 (31)	Neutral	Hepatic	3.2	37.4	0.735	(Mahmood and Balian, 1996)
26	Diltiazem	414.5	16 (35)	Base	Hepatic	25	62.8	0.888	(Evans et al., 2006)

27	Doxorubicin	543.5	13	Base	Hepatic	25	40.8	0.887	(Harris and Gross, 1975, Tranum et al., 1975)
28	Enoxacin	320.3	9.3 (14)	Acid	Mixed	69	0.353	1.51	(Nakamura et al., 1983, Chang et al., 1988)
29	Enprofylline	194.2	3.6 (24)	Base	Renal	49	6.34	0.526	(Tsunekawa et al., 1992)
30	Epiroprim	353.4	3.5 (17)	Acid	Mixed	12.5	34.4	0.609	(Evans et al., 2006)
31	Felodipine	384.3	11 (19)	Neutral	Hepatic	1	43.8	0.575	(Evans et al., 2006)
32	Fentanyl	336.5	11 (33)	Base	Hepatic	17	15.6	0.805	(Bjorkman and Redke, 2000, Valverde et al., 2000)
33	Flindokalner	359.7	7.6	Acid	Hepatic	0.38	21.9	0.629	(Evans et al., 2006)
34	Furosemide	330.7	2.3 (47)	Acid	Renal	5	3.78	1.11	(Doyle et al., 1982, Prandota and Pruitt, 1991, Hirai et al., 1992)
35	Garenoxacin	426.4	1.2	Acid	Mixed	13	5.78	0.605	(Evans et al., 2006)
36	GV150526	360.2	0.086 (24)	Acid	Hepatic	0.002	1.99	1.20	(Iavarone et al., 1999)
37	Haloperidol	375.9	12	Base	Hepatic	10	46.1	0.573	(Evans et al., 2006)
38	Imatinib	493.6	3.2 (34)	Base	Hepatic	5.9	29.6	0.866	(Neville et al., 2004, Peng et al., 2004, Ishizuka et al., 2007, Oostendorp et al., 2009)
39	Inogatran	439.0	5.8 (8.6)	Base	Renal	0.2	24.7	0.748	(Eriksson et al., 1998, Hauptmann, 2002)
40	ITF296	238.2	30 (20)	Acid	Hepatic	NA	40.8	1.05	(Monzani et al., 1995, Sardina et al., 1995, Giachetti et al., 1998, Monzani et al., 1999)
41	Ketoprofen	254.3	1.2 (68)	Acid	Hepatic	1	0.930	1.31	(Lepist and Jusko, 2004)
42	Ketorolac	376.4	0.80 (11)	Acid	Mixed	0.8	1.28	0.989	(Mroszczak et al., 1987)
43	Lamifiban	468.5	1.9	Zwitt	Renal	94	6.14	0.884	(Lave et al., 1996)
44	Meropenem	383.5	3.2 (16)	Acid	Mixed	98	17.7	0.418	(Harrison et al., 1989)
45	Methadone	429.6	1.4	Base	Mixed	20	43.5	0.775	(Evans et al., 2006)
46	Metoprolol	267.4	16 (53)	Base	Hepatic	88	137	0.426	(Rane et al., 1984, Belpaire et al., 1990, Bortolotti et al., 1989, Murthy et al., 1991)
47	Mibefradil	495.6	7.0	Acid	Hepatic	1	66.9	0.804	(Lave et al., 1997)
48	Midazolam	309.5	7.6 (5.9)	Neutral	Hepatic	4.0	42.4	0.737	(Evans et al., 2006)
49	Mifepristone	325.8	0.33	Base	Hepatic	2	34.7	0.720	(Evans et al., 2006, Kenny and Grime, 2006)
50	Mofarotene	433.6	11	Base	Hepatic	0.1	11.5	0.733	(Mahmood and Balian, 1996)
51	Moxalactam	520.5	1.6 (26)	Acid	Renal	40	4.97	0.651	(Mahmood and Balian, 1996)
52	Nicardipine	479.5	7.0	Base	Hepatic	1.5	63.1	0.727	(Higuchi and Shiobara, 1980)
53	Nifedipine	346.3	7.0	Neutral	Hepatic	5	6.12	1.24	(Evans et al., 2006)
54	Ofloxacin	361.4	4.5 (15)	Zwitt	Renal	75	9.44	0.569	(Evans et al., 2006)
55	Panipenem	339.4	3.1 (12)	Acid	Mixed	92.6	14.8	0.492	(Kurihara et al., 1992)
56	PD1	364.8	0.0043	Base	Hepatic	49	0.0276	0.966	(Feng et al., 2000)

57	PD8	245.3	1.6	Base	Renal	16	5.06	0.629	(Feng et al., 2000)
58	Phencyclidine	243.4	5.1 (22)	Base	Hepatic	35	76.3	0.763	(Bachmann, 1989)
59	PNU-96391	281.4	7.2 (38)	Base	Hepatic	0.73	41.7	0.923	(Evans et al., 2006)
60	PNU-288034	403.4	7.3	Base	Renal	NA	10.7	0.699	(Lai et al.)
61	Propafenone	341.5	18 (19)	Base	Hepatic	3	50.9	0.841	(Evans et al., 2006)
62	Propranolol	259.3	12 (7.7)	Base	Hepatic	8.4	47.7	0.652	(Mahmood and Balian, 1996)
63	Quinidine	324.4	3.8 (47)	Base	Hepatic	17.5	30.0	0.539	(Ueda et al., 1977, Guentert et al., 1982, Iven, 1977)
64	Remoxipride	371.3	1.7 (29)	Base	Hepatic	6.5	91.2	0.506	(Evans et al., 2006)
65	RO 24-6173	349.3	12	NA	Hepatic	10	68.8	0.716	(Lave et al., 1997)
66	RO 25-6833	560.5	0.39 (29)	Acid	Mixed	4.3	1.06	1.18	(Richter et al., 1998)
67	Salicylic acid	138.1	0.56	Acid	Hepatic	15	0.0554	1.63	(Davis and Westfall, 1972)
68	Sematilide	313.4	4.1 (14)	Base	Renal	96	19.7	0.727	(Hinderling et al., 1993)
69	Semaxanib	238.3	14 (50)	Base	Mixed	0.8	48.8	0.857	(Evans et al., 2006)
70	Stavudine	242.2	9.8 (39)	Base	Renal	100	20.8	0.909	(Kaul et al., 1999)
71	Susalimod	408.0	0.090	Acid	Hepatic	23.5	9.32	0.957	(Feng et al., 2000)
72	Tamsulosin	408.5	0.69	Base	Hepatic	1.0	61.1	0.594	(Bolton, 1997)
73	Tebufelone	300.4	9.9	Acid	Hepatic	0.001	31.1	0.878	(Cruze et al., 1995)
74	Theophylline	180.2	0.86 (28)	Acid	Hepatic	58	2.68	0.906	(Mahmood and Balian, 1996)
75	Tolcapone	273.2	1.5 (22)	Base	Hepatic	0.1	12.4	0.654	(Lave et al., 1997)
76	Trimethadione	143.1	0.70 (14)	Neutral	Hepatic	0.1	3.78	0.743	(Tanaka et al., 1999)
77	Troglitazone	441.5	2.5 (20)	Acid	Hepatic	1	12.5	0.795	(Izumi et al., 1996)
78	Valproate	144.2	0.11 (18)	Acid	Hepatic	5.2	3.61	0.947	(Bolton, 1997)
79	Verapamil	454.6	13 (31)	Base	Hepatic	10	40.7	1.08	(Evans et al., 2006)
80	Vinorelbine	778.9	19 (19)	Acid	Hepatic	9-21	25.8	0.915	(Evans et al., 2006)
81	Warfarin	308.3	0.058 (19)	Acid	Hepatic	1	0.382	1.20	(Bachmann, 1989)

Zwitt, zwitterion; NA, information not available