APPENDIX A: SUMMARY TABLES OF ANIMAL AND HUMAN STUIDES FROM THE COPPER TOXICITY DATABASE

Table A1: References and Observations on Copper Excess

Ref. (ID#)	*Test Type*	*Species*	*Strain*	*Copper Species*	*Route of Admin.*	*Life stage*	*Sex*	*Exp.*	*Grp.*	*Conc.*	*Days*	*Sev.*
Baker 1999a (2)	Subacute Toxicity	Human	NA	Copper sulfate	Capsule	Adult	M	1	1	0 mg/d	42	0
								1	2	3 mg/d	42	0
								1	3	6 mg/d	42	0
							F	2	1	0 mg/d	42	0
								2	2	3 mg/d	42	0
								2	3	6 mg/d	42	0
Pratt 1985 (6)	Subchronic Toxicity	Human	NA	Copper gluconate	Capsule	Adult	B	1	1	0 mg/d	84	0
								1	2	10 mg/d	84	2
Murthy 1981 (10)	Subacute Toxicity	Rats	NS	Copper sulfate pentahydrate	Feed	Adult	M	1	1	0 mg/d	30	0
								1	2	5 mg/d	30	3
Jones 1997 (14)	Subacute	Human	NA	Copper as glycine-chelate	Capsule	NS	M	1	1	0 mg/d	28	0
								1	2	2 mg/d	28	0
Haywood 1985 (20)	Subacute Toxicity	Rats	Wistar	NS	Feed	Weanling	M	1	1	10 mg/kg	7	0
								1	2	3000 mg/kg	7	1
								1	3	4000 mg/kg	7	1
								1	4	5000 mg/kg	7	1
								1	5	6000 mg/kg	7	4
								2	1	10 mg/kg	14	0
								2	2	3000 mg/kg	14	4
								2	3	4000 mg/kg	14	4
								2	4	5000 mg/kg	14	4
								2	5	6000 mg/kg	14	4
								3	1	10 mg/kg	21	0
								3	2	3000 mg/kg	21	4
								3	3	4000 mg/kg	21	4
								3	4	5000 mg/kg	21	4
								3	5	6000 mg/kg	21	4
								4	1	10 mg/kg	28	0
								4	2	3000 mg/kg	28	4

									4	3	4000 mg/kg	28	4
									4	4	5000 mg/kg	28	4
									4	5	6000 mg/kg	28	4
	Subchronic Toxicity								5	1	10 mg/kg	35	0
									5	2	3000 mg/kg	35	4
									5	3	4000 mg/kg	35	4
									5	4	5000 mg/kg	35	4
									5	5	6000 mg/kg	35	5
									6	1	10 mg/kg	42	0
									6	2	3000 mg/kg	42	4
									6	3	4000 mg/kg	42	4
									6	4	5000 mg/kg	42	4
									6	5	6000 mg/kg	42	5
	Chronic Toxicity								7	1	10 mg/kg	105	0
									7	2	3000 mg/kg	105	4
									7	3	4000 mg/kg	105	4
									7	4	5000 mg/kg	105	4
									7	5	6000 mg/kg	105	5
Haywood 1980 (22)	Subacute Toxicity	Rats	NS	Copper sulfate	Feed	Weanling	M	1	1	0 ppm	7	0
								1	2	2000 ppm	7	1
	Subacute Toxicity							2	1	0 ppm	14	0
								2	2	2000 ppm	14	4
	Subacute Toxicity							3	1	0 ppm	21	0
								3	2	2000 ppm	21	4
	Subchronic Toxicity							4	1	0 ppm	42	0
								4	2	2000 ppm	42	4
	Subchronic							5	1	0 ppm	63	0
								5	2	2000 ppm	63	4
	Chronic							6	1	0 ppm	105	0
								6	2	2000 ppm	105	4
Fuentealba 2000 (25)	Chronic	Rats	Fischer 344	Copper sulfate	Feed	Adult	M	1	1	0 ppm	126	0
								1	2	1500 ppm	126	3
							F	2	1	0 ppm	126	0

								2	2	1500 ppm	126	3
Hebert 1993 (26)	Subacute Toxicity	Rats	Fischer 344	Copper sulfate pentahydrate	Water	Adult	M	1	1	0 ppm	15	0
								1	2	300 ppm	15	0
								1	3	1000 ppm	15	0
								1	4	3000 ppm	15	3
								1	5	10000 ppm	15	6
								1	6	30000 ppm	15	6
	Subacute Toxicity	Mice	B6C3F1	Copper sulfate pentahydrate	Water	Adult	M	2	1	0 ppm	15	0
								2	2	300 ppm	15	0
								2	3	1000 ppm	15	0
								2	4	3000 ppm	15	4
								2	5	10000 ppm	15	6
								2	6	30000 ppm	15	6
	Subacute Toxicity	Rats	Fischer 344	Copper sulfate pentahydrate	Water	Adult	F	3	1	0 ppm	15	0
								3	2	300 ppm	15	0
								3	3	1000 ppm	15	0
								3	4	3000 ppm	15	3
								3	5	10000 ppm	15	6
								3	6	30000 ppm	15	6
	Subacute Toxicity	Mice	B6C3F1	Copper sulfate pentahydrate	Water	Adult	F	4	1	0 ppm	15	0
								4	2	300 ppm	15	0
								4	3	1000 ppm	15	3
								4	4	3000 ppm	15	4
								4	5	10000 ppm	15	6
								4	6	30000 ppm	15	6
	Subacute Toxicity	Rats	Fischer 344	Copper sulfate pentahydrate	Feed	Adult	M	5	1	0 ppm	15	0
								5	2	1000 ppm	15	0
								5	3	2000 ppm	15	0
								5	4	4000 ppm	15	0
								5	5	8000 ppm	15	4
								5	6	16000 ppm	15	4
	Subacute Toxicity	Rats	Fischer 344	Copper sulfate pentahydrate	Feed	Adult	F	6	1	0 ppm	15	0
								6	2	1000 ppm	15	0

							6	3	2000 ppm	15	0
							6	4	4000 ppm	15	3
							6	5	8000 ppm	15	4
							6	6	16000 ppm	15	4
Subacute Toxicity	Mice	B6C3F1	Copper sulfate pentahydrate	Feed	Adult	M	7	1	0 ppm	15	0
							7	2	1000 ppm	15	0
							7	3	2000 ppm	15	0
							7	4	4000 ppm	15	4
							7	5	8000 ppm	15	4
							7	6	16000 ppm	15	4
Subacute Toxicity	Mice	B6C3F1	Copper sulfate pentahydrate	Feed	Adult	F	8	1	0 ppm	15	0
							8	2	1000 ppm	15	0
							8	3	2000 ppm	15	0
							8	4	4000 ppm	15	4
							8	5	8000 ppm	15	4
							8	6	16000 ppm	15	4
Subchronic Toxicity	Rats	Fischer 344	Copper sulfate pentahydrate	Feed	Adult	M	9	1	0 ppm	92	0
							9	2	500 ppm	92	1
							9	3	1000 ppm	92	3
							9	4	2000 ppm	92	4
							9	5	4000 ppm	92	4
							9	6	8000 ppm	92	4
Subchronic Toxicity	Rats	Fischer 344	Copper sulfate pentahydrate	Feed	Adult	F	10	1	0 ppm	92	0
							10	2	500 ppm	92	1
							10	3	1000 ppm	92	3
							10	4	2000 ppm	92	4
							10	5	4000 ppm	92	4
							10	6	8000 ppm	92	4
Chronic Toxicity	Mice	B6C3F1	Copper sulfate pentahydrate	Feed	Adult	M	11	1	0 ppm	92	0
							11	2	1000 ppm	92	0
							11	3	2000 ppm	92	0
							11	4	4000 ppm	92	4
							11	5	8000 ppm	92	4

								11	6	16000 ppm	92	4
	Chronic Toxicity	Mice	B6C3F1	Copper sulfate pentahydrate	Feed	Adult	F	12	1	0 ppm	92	0
								12	2	1000 ppm	92	0
								12	3	2000 ppm	92	0
								12	4	4000 ppm	92	4
								12	5	8000 ppm	92	4
								12	6	16000 ppm	92	4
Araya 2001 (35)	Acute Toxicity	Human	NA	Copper sulfate pentahydrate	Water	Adult	B	1	1	0 mg/L	1	0
								1	2	2 mg/L	1	0
								1	3	4 mg/L	1	0
								1	4	6 mg/L	1	4
								1	5	8 mg/L	1	4
Baker 1999b (37)	Subacute Toxicity	Humans	NA	Copper sulfate pentahydrate	Diet	Adult	M	1	1	1.6 mg/day	42	0
										6.0 mg/day	42	0
Cristofori 1992 (42)	Chronic Toxicity	Rats	Spraque-Dawley	NS	Diet	Adult	F	1	1	5 ppm	210	0
								1	2	200 ppm	210	2
	Chronic Toxicity	Rats	Spraque-Dawley	NS	Diet	Adult	F	2	1	5 ppm	350	0
								2	2	200 ppm	350	2
Cromwell 1989 (43)	Subacute Toxicity	Pig	Hamshire-Yorkshire	Copper sulfate pentahydrate	Diet	Weanling	B	1	1	0 ppm	28	0
								1	2	125 ppm	28	3
								1	3	250 ppm	28	3
				Copper Oxide				2	1	0 ppm	28	0
								2	2	125 ppm	28	0
								2	3	250 ppm	28	0
Cunnane 1985 (44)	Subchronic Toxicity	Rats	Sprague-Dawley	NS	Diet	Weaning	M	1	1	6 mg/kg/d	84	0
								1	2	250 mg/kg/d	84	3
Fuentealba 1989 (48)	Subacute Toxicity	Rats	Wistar	NS	Diet	Weaning	M	1	1	20 ppm	7	0
								1	2	1500 ppm	7	4
								2	1	20 ppm	28	0
								2	2	1500 ppm	28	4
	Subchronic Toxicity							3	1	20 ppm	56	0
								3	2	1500 ppm	56	4
								4	1	20 ppm	84	0

								4	2	1500 ppm	84	4
	Chronic Toxicity							5	1	20 ppm	112	0
								5	2	1500 ppm	112	4
Giovanetti 1998 (50)	Subacute Toxicity	Mice	B6C3F1	Copper sulfate pentahydrate	Diet	Weaning	M	1	1	4.98 ppm	28	0
								1	2	200 ppm	28	3
Gotteland 2001 (54)	Acute Toxicity	Humans	NS	Copper sulfate pentahydrate	Water	Adults	B	1	1	10 mg/L	1	4
Greene 1987 (55)	Chronic Toxicity	Rats	Sprague-Dawley	NS	Diet	Weaning	M	1	1	25 ppm	112	0
										100 ppm	112	0
Gross 1989 (56)	Chronic Toxicity	Rats	Sprague-Dawley	Copper acetate	Water	Adult	M	1	1	0 %	252	0
								1	2	0.0125 %	252	3
Jantsch 1985(63)	Acute Toxicity	Human	NA	Copper sulfate pentahydrate	Diet	Adult	M	1	1	250 g/day	1	4
Liu 1986 (75)	Chronic Toxicity	Rats	Wistar	Copper carbonate	Diet	Weaning	M	1	1	18 mg/kg/d	105	0
								1	2	100 mg/kg/d	105	3
Mullins 1998 (80)	Subchronic Toxicity	Rats	Wistar	Copper sulfate pentahydrate	Diet	Adults	M	1	1	10 mg/kg	42	0
								1	2	1500 mg/kg	42	2
O'Donohue 1999 (82)	Chronic Toxicity	Humans	NS	NS	Capsule	Adults	M	1	1	45 mg/day	1095	4
Zhang 2000 (98)	Subchronic Toxicity	Rats	Wistar	Copper sulfate pentahydrate	Capsule	Adult	B	1	1	0 mg/kg/d	40	0
								1	2	500 mg/kg/d	40	3
Rana 1980 (99)	Subacute	Rats	NS	Copper sulfate pentahydrate	Diet	Adult	M	1	1	0 mg/kg/day	20	0
								1	2	100 mg/kg/day	20	4
Massie 1984 (103)	Chronic Toxicity	Mice	C57B1/6J	Cu gluconate	Water	Adult	M	1	1	0 ppm	NA[a]	0
								1	2	317 ppm	NA[a]	6
Pizarro 1999b (104)	Subchronic Toxicity	Human	NA	Copper sulfate pentahydrate	Water	Adult	F	1	1	0 mg/L	77	0
								1	2	1 mg/L	77	0
								1	3	3 mg/L	77	4
								1	4	5 mg/L	77	4
Araya 2003a (109)	Acute Toxicity	Humans	NA	Copper sulfate pentahydrate	Water	Adult	B	1	1	0 mg/l	1	0
								1	2	10 mg/l	1	4
Araya 2003b (110)	Acute Toxicity	Humans	NA	Copper sulfate pentahydrate	Water	Adult	F	1	1	0 mg/l	1	0
								1	2	2 mg/l	1	0
								1	3	4 mg/l	1	0
								1	4	6 mg/l	1	4
								1	5	8 mg/l	1	4

Araya 2003c (111)	Subchronic Toxicity	Humans	NA	Copper sulfate pentahydrate	Water	Adult	B	1	1	0.01 mg/l	60	0
								1	2	2 mg/l	60	0
								1	3	4 mg/l	60	0
								1	4	6 mg/l	60	4
Araya 2004 (112)	Subchronic Toxicity	Humans	NA	Copper sulfate pentahydrate	Water	Adult	B	1	1	0 mg/l	60	0
								1	2	2 mg/l	60	0
								1	3	4 mg/l	60	4
								1	4	5 mg/l	60	4
Armstrong 2004 (114)	Subchronic	Pigs	NS	Copper sulfate pentahydrate	Feed	Weanling	**B**	1	1	10 ppm	40	0
								1	2	135 ppm	40	3
								1	3	260 ppm	40	3
				Copper citrate				2	1	15 ppm	40	0
								2	2	46 ppm	40	0
								2	3	77 ppm	40	0
								2	4	140 ppm	40	3
Cisternas 2005 (117)	Chronic	Rats	Sprague-Dawley	Copper sulfate pentahydrate	Feed	Weanling	B	1	1	10 ppm	120	0
								1	2	1200ppm	120	4
Feng 2007 (126)	Subacute	Pigs	NS	Copper sulfate pentahydrate	Feed	NS	B	1	1	12.4 mg/kg	30	0
								1	2	250 mg/kg	30	2
								2	1	12.4 mg/kg	30	0
				Copper Proteinate				2	2	50 mg/kg	30	0
								2	3	100 mg/kg	30	2
Kvietkauskaite 2004 (136)	Subchronic	Mice	BALB/c	Copper sulfate pentahydrate	Water	Adults	M	1	1	0 mg/kg bw/d	133	0
								1	2	22 mg/kg bw/d	133	3
								1	3	42 mg/kg bw/d	133	3
O'Connor 2003 (138)	Subacute	Humans	NA	Copper sulfate pentahydrate	Capsule	Adult	B	1	1	1.23 mg/d	42	0
								1	2	4.23 mg/d	42	1
				Copper glycine chelates				2	1	1.23 mg/d	42	0
								2	2	4.23 mg/d	42	1
								3	1	1.23 mg/d	42	0
								3	2	7.23 mg/d	42	1
Ozcelik 2002 (140)	Subchronic	Rats	Wistar albino	Copper sulfate pentahydrate	Water	Adult	B	1	1	0 μg/mL	54	0
								1	2	250 μg/mL	54	3

Turnlund 2004 (146)	Subacute	Humans	NA	NS	Supplement	Adult	M	1	1	7.8 mg/d	18	2
Alissa 2004 (152)	Subchronic	Rabbits	New Zealand White	NS	Feed	Adult	M	1	1	3.7 mg/d	84	0
								1	2	350 mg/d	84	3
Becaria 2006 (158)	Subchronic	Mice	B6C3F1	Copper sulfate pentahydrate	Water	Adult	M	1	1	0 ppm	84	0
								1	2	2 ppm	84	3
Davis 2002 (172)	Subacute	Pigs	NS	NS	Feed	Weanling	B	1	1	20 ppm	10	0
								1	2	195 ppm	10	3
Goldschmith 2005 (178)	Subacute	Rats	NS	Copper sulfate pentahydrate	Water	Adult	B	1	1	0.12 mg/d	20	0
								1	2	12.12 mg/d	20	4
Gurel 2007 (180)	Subchronic	Rats	Sprague-Dawley	NS	Water	Adult	F	1	1	0 mg/l	60	0
								1	2	100 mg/l	60	4
								1	3	400 mg/l	60	4
Lai 2005 (187)	Subacute	Rats	Wistar	Copper sulfate pentahydrate	Water	Weanling	M	1	1	0 μg/mL	7	0
								1	2	50 μg/mL	7	0
								1	3	100 μg/mL	7	0
								1	4	200 μg/mL	7	3

[a]Exposure duration = lifespan of each subject 500-975.

Note. Ref. (ID#), reference and identification number; M, male; F, female; B, male and female; Exp., experiment number within the publication; Grp., group number within the experiment; Conc., concentration reported in the study; Sev., severity score assigned.

Table A2: References and Observations on Copper Deficiency

Ref (ID#)	*Exposure Duration Categories*	*Species*	*Strain*	*Copper Species*	*Route of Admin.*	*Life stage*	*Sex*	*Exp.*	*Grp.*	*Conc.*	*Days*	Sev
Arce 1992 (1)	Subchronic	Mice	Swiss Webster	Copper Sulfate	Feed	Adult	F	1	1	1 ppm	39	2
								1	2	10 ppm	39	0
DiSilvestro 1992 (4)	Subchronic	Rats	Sprague-Dawley	Copper Sulfate	Feed	Postweanling	M	1	1	8 ppm	42	0
								1	2	2.5 ppm	42	2
								1	3	0.2 ppm	42	3
Klevay 1985 (8)	Chronic	Mice	Swiss Webster	Copper sulfate pentahydrate	Water	Adult	F	1	1	0 µg/ml	NA[a]	3
								1	2	10 µg/ml	NA[a]	0
Schuschke 1999 (16)	Subacute	Rats	Sprague-Dawley	Copper sulfate pentahydrate	Feed	Weaning	M	1	1	0 ppm	28	3
								1	2	1.5 ppm	28	3
								1	3	3 ppm	28	3
								1	4	6 ppm	28	0
Schuschke 1995 (17)	Subacute	Rats	Sprague-Dawley	NS	Feed	Weaning	M	1	1	6 ppm	7	0
								1	2	3 ppm	7	1
								1	3	1.5 ppm	7	3
								2	1	1.5 ppm	21	3
								2	2	3 ppm	21	1
								2	3	6 ppm	21	0
								3	1	1.5 ppm	35	3
								3	2	3 ppm	35	3
								3	3	6 ppm	35	0
Kelley 1995 (18)	Subacute	Human	NA	NS	Diet	Young adults	M	1	1	0.66 mg/d	24	2
Prohaska 1995 (19)	Subchronic	Rats	Sprague-Dawley	Copper sulfate	Water	Weanling	M	1	1	0 mg/L	38.5	3
								1	2	20 mg/L	38.5	0
Saari 1999 (24)	Subchronic	Rats	Sprague-Dawley	NS	Feed	Weanling	M	1	1	6 ppm	35	0
								1	2	0.8 ppm	35	3
								1	3	0.4 ppm	35	3
								1	4	0 ppm	35	3
Menino 1986 (27)	Subchronic	Mice	Swiss-Webster	Copper carbonate	Feed	Adult	F	1	1	11 ppm	60	0
								1	2	6 ppm	60	0

								1	3	5 ppm	60	0
								1	4	4 ppm	60	0
								1	5	3 ppm	60	3
								1	6	2 ppm	60	4
								1	7	1 ppm	60	4
Turnlund 1990 (31)	Subchronic	Humans	NA	Copper sulfate pentahydrate	Diet	Adult	M	1	1	0.785 mg/d	90	1
								1	2	1.68 mg/d	90	0
Allen 1996 (32)	Chronic	Rats	Sprague-Dawley	Copper carbonate	Diet	Weaning	M	1	1	5.79 mg/kg	140	0
								1	2	0.46 mg/kg	140	3
Allen 1978 (33)	Subchronic	Rats	Sprague-Dawley	Copper sulfate pentahydrate	Diet	Weaning	M	1	1	0.57 µg	63	3
								1	2	5 µg	63	0
Allen 1988 (34)	Subchronic	Rats	Rowett	NS	Diet	Weaning	M	1	1	0.2 µg	49	2
								1	2	10 µg	49	0
Baker 1999b (37)	Subchronic	Human	NA	Copper sulfate pentahydrate	Diet	Adult	M	1	1	1.6 mg/d	42	0
								1	2	0.7 mg/d	42	2
Bala 1990 (38)	Subchronic	Rats	Lewis	Copper carbonate	Diet	Weaned	M	1	1	0.6 µg/g	35	3
								1	2	6 µg/g	35	0
						Birth-5weeks post weanling	M	2	1	0.6 µg/g	56	2
								2	2	6 µg/g	56	0
Bala 1992 (39)	Subchronic	Pig	NS	NS	Diet	Weanling	B	1	1	0.8 mg/kg/d	77	3
								1	2	6.4 mg/kg/d	77	0
Bode 1992 (40)	Subacute	Rats	Sprague-Dawley	Copper sulfate pentahydrate	Diet	Weanling	M	1	1	0.4 g/kg	28	3
								1	2	5.2 g/kg	28	0
Bremner 1987 (41)	Subchronic	Rats	Hooded Lister	Copper sulfate pentahydrate	Diet	Post-weanling	M	1	1	0.15 mg/kg/d	42	3
								1	2	10 mg/kg/d	42	0
Cunnane 1985 (44)	Subchronic	Rats	Sprague-Dawley	NS	Diet	Weaning	M	1	1	1 mg/kg/d	84	3
								1	2	6 mg/kg/d	84	0
Davidson 1992 (45)	Subchronic	Rats	Sprague-Dawley	Copper carbonate	Diet	Weanling	M	1	1	6.2 µmol/kg	35	3
								1	2	92.4 µmol/kg	35	0
Fields 1997 (47)	Subacute	Rats	Sprague-Dawley	NS	Diet	Weanling	B	1	1	0.6 µg/g	28	3
								1	2	6 µg/g	28	0
Giovanetti 1998 (50)	Subacute	Mice	B6C3F1	Copper sulfate pentahydrate	Diet	Weanling	M	1	1	0.44 ppm	28	3
								1	2	4.98 ppm	28	0

Gitlin 1992 (51)	Subacute	Rats	Sprague-Dawley	NS	Diet	Adult	B	1	1	0.6 mg/kg/d	28	2
								1	2	6 mg/kg/d	28	0
Gomi 1995 (52)	Subchronic	Rats	Fischer 344	Copper oxide	Diet	Adult	F	1	1	0.4 mg/kg/d	70	2
								1	2	5.7 mg/kg/d	70	0
						Adult		2	1	0.4 mg/kg/d	70	3
								2	2	5.7 mg/kg/d	70	0
Goodman 1970 (53)	Subchronic	Rats	Wistar	Copper sulfate pentahydrate	Water	Weanling	M	1	1	0 mg/L	60	3
								1	2	40 mg/L	60	0
Greene 1987 (55)	Chronic	Rats	Sprague-Dawley	NS	Diet	Weanling	M	1	1	0.6 ppm	112	4
								1	2	25 ppm	112	0
Hamilton 2000 (58)	Subchronic	Mice	C57846	NS	Diet	Weaning	M	1	1	0.6 mg/kg/d	98	4
								1	2	2 mg/kg/d	98	4
								1	3	6 mg/kg/d	98	0
Hopkins 1995 (62)	Chronic	Rats	Sprague-Dawley	Copper carbonate	Diet	Weanling	B	1	1	2.8 mg/kg/d	161	3
								1	2	6.6 mg/kg/d	161	0
Johnson 1993 (66)	Subchronic	Rats	Sprague-Dawley	NS	Diet	Weanling	M	1	1	0.2 µg/g	35	3
								1	2	1 µg/g	35	3
								1	3	2 µg/g	35	2
								1	4	3 µg/g	35	2
								1	5	4 µg/g	35	0
Kang 2000 (67)	Subchronic	Mice	FVB	NS	Diet	Weanling	B	1	1	0.35 mg/kg/d	35	3
								1	2	6 mg/kg/d	35	0
Karimbakas 1998 (68)	Subacute	Mice	ICR	NS	Diet	Weanling	M	1	1	1.05 µg/g	21	3
								1	2	6.4 µg/g	21	0
Klevay 1981 (70)	Subchronic	Rats	Sprague-Dawley	Copper sulfate pentahydrate	Diet	Weanling	M	1	1	0.79 µg/g	35	6
								1	2	3.79 µg/g	35	0
Klevay 1986 (71)	Subchronic	Humans	NA	NS	Diet	Adults	M	1	1	0.78 mg/d	150	3
Lai 1995 (72)	Subacute	Rats	Sprague-Dawley	Copper sulfate pentahydrate	Water	Weanling	M	1	1	0 µg/ml	28	3
								1	2	3 µg/ml	28	0
Lai 1994 (73)	Subacute	Rats	Sprague-Dawley	Copper sulfate pentahydrate	Water	Weanling	M	1	1	0 µg/ml	28	2
								1	2	3 µg/ml	28	0
Lai 1996 (74)	Subacute	Rats	Sprague-Dawley	Copper sulfate pentahydrate	Water	Weanling	M	1	1	0 µg/ml	28	3
								1	2	3 µg/ml	28	0

Lynch 1994 (76)	Subchronic	Mice	Swiss-Webster	NS	Diet	Adults	B	1	1	0.3 mg/kg/d	49	3
								1	2	8.4 mg/kg/d	49	0
Mao 1998 (77)	Subchronic	Rats	Sprague-Dawley	NS	Diet	Weanling	M	1	1	1 mg/kg/d	77	3
								1	2	7 mg/kg/d	77	0
Mao 1999 (78)	Subchronic	Rats	Long-Evans	Copper carbonate	Diet	Weanling	M	1	1	2.7 mg/kg/d	84	3
								1	2	6.2 mg/kg/d	84	0
Nelson 1992 (81)	Subacute	Rats	Sprague-Dawley	NS	Feed	Weanling	M	1	1	0.8 mg/kg/d	42	3
								1	2	1.7 mg/kg/d	42	3
								1	3	6.7 mg/kg/d	42	0
Olin 1994 (83)	Subacute	Rats	Sprague-Dawley	NS	Diet	Weanling	B	1	1	7.9 nmol/g	21	3
								1	2	125.9 nmol/g	21	0
Prohaska 2001 (84)	Subacute	Rats	Sprague-Dawley	Copper sulfate pentahydrate	Water	Weaning	F	1	1	20 mg/L/d	30	0
								1	2	0 mg/L/d	30	3
Prohaska 1982 (85)	Subchronic	Rats	Sprague-Dawley	Copper sulfate pentahydrate	Water	Weanling	M	1	1	0 ppm	35	3
								1	2	20 ppm	35	0
Prohaska 1994 (86)	Subacute	Rats	Sprague-Dawley	Copper sulfate pentahydrate	Diet	Infant	B	1	1	0.4 mg/kg/day	28	3
								1	2	4 mg/kg/day	28	0
Rock 1995 (89)	Subchronic	Rats	Wistar	Copper carbonate	Diet	Weanling	M	1	1	0.6 mg/kg/d	42	3
								1	2	7.5 mg/kg/d	42	0
Saari 2002a (90)	Subchronic	Rats	Sprague-Dawley	Copper sulfate pentahydrate	Diet	Weanling	M	1	1	0.27 mg/kg/d	35	3
								1	2	1.43 mg/kg/d	35	2
								1	3	2.92 mg/kg/d	35	2
								1	4	4.27 mg/kg/d	35	0
								1	5	6.15 mg/kg/d	35	0
Saari 2002b (91)	Subchronic	Rats	Sprague-Dawley	Copper sulfate pentahydrate	Diet	Weanling	M	1	1	0 mg/kg/d	35	3
								1	2	1.6 mg/kg/d	35	1
								1	3	3.2 mg/kg/d	35	1
								1	4	24 mg/kg/d	35	0
Sugawara 1999 (92)	Subchronic	Rats	Long-Evans	Copper chloride	Diet	Adults	B	1	1	0.5 mg/kg/d	35	2
								1	2	10 mg/kg/d	35	0
Wang 1996 (95)	Subchronic	Rats	Sprague-Dawley	Copper carbonate	Diet	Weaning	M	1	1	9.4 μmol/kg	42	3
								1	2	103.9 μmol/kg	42	0
Wildman 1995 (96)	Chronic	Rats	Sprague-Dawley	NS	Diet	Weaning	M	1	1	1.3 mg/kg/d	154	3

								1	2	2.8 mg/kg/d	154	3
								1	3	6.7 mg/kg/d	154	0
Rayssiguier 1993 (100)	Subchronic	Rats	Wistar	Copper carbonate	Diet	Weaning	M	1	1	0.6 mg/kg/d	42	3
								1	2	7.5 mg/kg/d	42	0
Reiser 1987 (102)	Subchronic	Humans	NA	NS	Diet	Adult	M	1	1	0.36mg/1000kcal	98	2
								1	2	0.57mg/1000 kcal	98	0
Allen 1978 (106)	Chronic	Rats	Sprague-Dawley	Copper sulfate pentahydrate	Diet	Weanling	M	1	1	0.57 μg/g	168	2
								1	2	5 μg/g	168	0
Ajayi 2005 (107)	Subchronic	Rats	White Albino	Copper carbonate	Diet	Weanling	M	1	1	0.06 mg/kg	42	3
								1	2	20.03 mg/kg	42	0
Andersen 2007 (108)	Subchronic	Rats	Rowett Lister	Copper sulfate pentahydrate	Diet	Weanling	F	1	1	5 mg/kg	49	0
								1	2	2.5 mg/kg	49	3
								1	3	0.75 mg/kg	49	3
Auclair 2006 (115)	Subchronic Toxicity	Mice	C57BL6	Cupric carbonate	Feed	Adults	M	1	1	6 ppm	84	0
								1	2	0.5 ppm	84	3
Cockell 2002 (118)	Subacute Toxicity	Rats	Long Evans	NS	Feed	Weanling	M	1	1	6.19 mg/kg	28	0
								1	2	0.43 mg/kg	28	3
Cockell 2005 (119)	Subacute Toxicity	Rats	Long Evans	NS	Feed	Weanling	M	1	1	6 mg/kg	30	0
								1	2	0.5 mg/kg	30	3
Lucca 2002 (120)	Subacute Toxicity	Rats	Sprague-Dawley	Copper sulfate pentahydrate	Feed	Weanling	M	1	1	5.6 mg/kg	30	0
								1	2	0.66 mg/kg	30	4
Davis 2002 (121)	Subacute Toxicity	Rats	Fisher 344	NS	Feed	Weanling	M	1	1	5.3 μg/g	28	0
								1	2	0.8 μg/g	28	2
Davis 2003 (122)	Subacute Toxicity	Humans	NS	Copper sulfate pentahydrate	Diet	Adults	M	1	1	2.59 mg/d	42	0
								1	2	0.59 mg/d	42	3
Dong 2005 (123)	Subchronic toxicity	Rats	Sprague-Dawley	Copper sulfate pentahydrate	Feed	Weanling	M	1	1	6 mg/kg	35	0
								1	2	0.5 mg/kg	35	4
Falcone 2005 (125)	Chronic Toxicity	Rats	Sprague-Dawley	Copper sulfate pentahydrate	Feed	Adult	M	1	1	5.88 mg/kg	180	0
								1	2	2.94 mg/kg	180	0
								1	3	1.62 mg/kg	180	1
Harvey 2003 (129)	Subacute Toxicity	Humans	NA	Copper chloride	Diet	Adult	M	1	1	6.0 mg/d	56	0
								1	2	1.6 mg/d	56	1
								1	3	0.7 mg/d	56	1

Johnson 2005 (133)	Subchronic Toxicity	Rats	Sprague-Dawley	Copper sulfate pentahydrate	Feed	Weanling	M	1	1	6 mg/kg	42	0
								1	2	3 mg/kg	42	1
								1	3	2.5 mg/kg	42	1
								1	4	2 mg/kg	42	1
								1	5	1.5 mg/kg	42	2
								1	6	1 mg/kg	42	2
								1	7	0.63 mg/kg	42	3
							F	2	1	6 mg/kg	42	0
								2	2	3 mg/kg	42	0
								2	3	2.5 mg/kg	42	1
								2	4	2 mg/kg	42	1
								2	5	1.5 mg/kg	42	2
								2	6	1 mg/kg	42	2
								2	7	0.63 mg/kg	42	3
Li 2005 (137)	Chronic	Rats	Sprague-Dawley	NS	Feed	Adults	M	1	1	5.7 mg/kg	470	0
								1	2	3.1 mg/kg	470	4
								1	3	1.65 mg/kg	470	4
Prohaska 2003 (141)	Subchronic	Mice	Swiss Webster	Copper sulfate pentahydrate	Feed	Adult	F	1	1	20 mg/L	35	0
								1	2	0 mg/L	35	3
		Rats	Holtzman			Adult	F	2	1	20 mg/L	35	0
								2	2	0 mg/L	35	2
Saari 2002 (142)	Subacute	Rats	Sprague-Dawley	Copper sulfate pentahydrate	Feed	Weanling	M	1	1	7.28 mg/kg	35	0
								1	2	2.45 mg/kg	35	3
								1	3	0.79 mg/kg	35	3
								1	4	0.37 mg/kg	35	3
Saari 2007 (143)	Subchronic	Rats	Sprague-Dawley	Copper sulfate pentahydrate	Feed	Weanling	M	1	1	6 mg/kg	35	0
								1	2	0.3 mg/kg	35	3
Schuschke 2002 (144)	Subacute	Rats	Sprague-Dawley	Copper sulfate pentahydrate	Feed	Weanling	M	1	1	6.18 mg/kg	28	0
								1	2	0.29 mg/kg	28	3
Welch 2007 (148)	Subchronic	Rats	Sprague-Dawley	NS	Feed	Weanling	M	1	1	10.5 mg/kg	60	0
								1	2	0.43 mg/kg	60	3
Zeng 2007 (149)	Subchronic	Rats	Sprague-Dawley	Copper sulfate pentahydrate	Feed	Weanling	M	1	1	6.26 mg/kg	35	0
								1	2	0.16 mg/kg	35	3

Chen 2002 (167)	Subchronic	Rats	Long Evans	NS	Feed	Weanling	M	1	1	7.19 mg/kg	35	0
								1	2	0.78 mg/kg	35	3
Gobejishvili 2002 (177)	Subacute	Rats	Sprague-Dawley	Copper sulfate pentahydrate	Feed	Weanling	M	1	1	5.6 mg/kg	28	0
								1	2	0.33 mg/kg	28	4
Gordon 2005 (179)	Subacute	Rats	Sprague-Dawley	Copper sulfate pentahydrate	Feed	Weanling	M	1	1	6.18 mg/kg	28	0
								1	2	0.29 mg/kg	28	3
Johnson 2004 (183)	Subchronic	Rats	Sprague-Dawley	Copper sulfate pentahydrate	Feed	Weanling	M	1	1	5.4 mg/kg	35	0
								1	2	0.3 mg/kg	35	3
Klaahsen 2007 (185)	Subacute	Rats	Long Evans	Cupric carbonate	Feed	Weanling	M	1	1	6 mg/kg	35	0
								1	2	0 mg/kg	35	3
Reeves 2005 (202)	Subacute	Rats	Sprague-Dawley	NS	Feed	Weanling	M	1	1	5.0 mg/kg	19	0
								1	2	0.25 mg/kg	19	3
							F	2	1	5.0 mg/kg	19	0
								2	2	0.25 mg/kg	19	3
Smith 2002 (211)	Subchronic	Rats	Sprague-Dawley	NS	Feed	Adult	M	1	1	5.7 mg/kg	49	0
								1	2	1.1 mg/kg	49	3

[a]Exposure duration = lifespan of each subject 500-975.

Note. Ref. (ID#), reference and identification number; M, male; F, female; B, male and female; Exp., experiment number within the publication; Grp., group number within the experiment; Conc., concentration reported in the study; Sev., severity score assigned.

APPENDIX E: ESTIMATES & ASSUMPTIONS TO DEFINE COPPER INTAKE & BODYWEIGHT

Table E1: Estimates and Assumptions for Copper Intake and Bodyweight – Copper Excess

ID#	*Weight at T1 (kg)*	*Age at T1 (days)*	*Exposure T (days)*	*Weight at T2*	*Age at T2*	*Age at Midpoint (days)*	*Weight at Midpoint (kg)*	*Consumption Feed (g)*	*Consumption water (ml)*
2	82.2	NA	42	NA	NS	NA	82.2	NA	NA
2	61.3	NA	42	NA	NS	NA	61.3	NA	NA
No need to estimate amount of copper in feed consumed – exposure was given via a capsule with copper content reported in milligrams per day. Weight and age is assumed to be constant from the beginning to the end of the study.									
6	**70**	NA	84	NA	NS	NA	**70**	NA	NA
Weight not given but assumed to be 70 kg. No need to estimate amount of copper in feed consumed – exposure was given via a capsule with copper content reported in milligrams.									
10	0.06	**27**	30	NS	**57**	**42**	**0.165**	**18**	NA
Weight reported at onset. Age and weight at mid-point estimated from Poiley (1972) based on specie, strain and weight. Consumption of feed derived from the NAS (1972) estimates by species, sex and weight.									
14	**70**	NS	28	NA	NA	NS	**70**	NA	NA
Weight at onset assumed to be 70kg for adult male. Weight and age is assumed to be constant from the beginning to the end of the study. Amount of copper consumed provided in the article.									
20	NS	**21**	7	NS	**28**	**24.5**	**0.069**	**9**	NA
20	NS	**21**	14	NS	**35**	**28**	**0.080**	**12**	NA
20	NS	**21**	21	NS	**42**	**31.5**	**0.100**	**15**	NA
20	NS	**21**	28	NS	**49**	**35**	**0.120**	**16**	NA
20	NS	**21**	35	NS	**56**	**38.5**	**0.139**	**17**	NA
20	NS	**21**	42	NS	**63**	**42**	**0.159**	**18**	NA
20	NS	**21**	105	NS	**126**	**73.5**	**0.326**	**20**	NA
Animals reported as being in the weaning stage. Estimate of 21 days for the age of weaning rats derived from the CCAC (1984). Weight at midpoint estimated from Poiley (1972) based on specie, strain and age. Consumption of feed based on NAS (1972).									
22	NS	**21**	7	NS	**28**	**24.5**	**0.069**	**9**	**NA**
22	NS	**21**	14	NS	**35**	**28**	**0.080**	**12**	**NA**
22	NS	**21**	21	NS	**42**	**31.5**	**0.997**	**15**	**NA**
22	NS	**21**	42	NS	**63**	**42**	**0.120**	**18**	**NA**

22	NS	**21**	63	NS	**84**	**52.5**	**0.213**	**19**	**NA**
22	NS	**21**	105	NS	**126**	**73.5**	**0.326**	**20**	**NA**
Animals reported as being in the weaning stage. Estimate of 21 days for the age of weaning rats derived from the CCAC (1984). Weight at midpoint estimated from Poiley (1972) based on specie, strain and age. Consumption of feed derived from the NAS (1972).									
25	NS	**72**	126	NS	**198**	**135**	**0.312**	**20**	**43.68**
25	NS	**72**	126	NS	**198**	**135**	**0.211**	**16**	**29.54**
Animals reported as being 'adults'. Estimate of 72 days for the age of adult rats derived from the CCAC (1984). Weight at midpoint estimated from Poiley (1972) based on specie, strain and age. Consumption of feed based on NAS (1972) and consumption of water derived from the CCAC (1984).									
26	0.083	**36**	15	NA	**51**	**43.5**	**0.105**	NA	NA
26	0.025	**42**	15	NA	**57**	**49.5**	**0.024**	NA	NA
26	0.088	**42**	15	NA	**57**	**49.5**	**0.111**	NA	NA
26	0.02	**35**	15	NA	**50**	**42.5**	**0.023**	NA	NA
26	0.107	**42**	15	NA	**57**	**49.5**	**0.154**	NA	NA
26	0.098	**46**	15	NA	**61**	**53.5**	**0.120**	NA	NA
26	0.022	**36**	15	NA	**51**	**43.5**	**0.023**	NA	NA
26	0.018	**32**	15	NA	**47**	**39.5**	**0.022**	NA	NA
26	0.119	**32**	91	NA	**123**	**77.5**	**0.335**	NA	NA
26	0.106	**31**	91	NA	**122**	**76.5**	**0.240**	NA	NA
26	0.021	**54**	91	NA	**145**	**99.5**	**0.030**	NA	NA
26	0.017	**49**	91	NA	**140**	**94.5**	**0.026**	NA	NA
Age estimated from Poiley (1972) based on specie, strain and body weight. Weight at midpoint estimated from Poiley (1972) based on specie, strain and age. Estimates of feed and water intake not needed as study provides detailed information on amount of copper consumed.									
35	**70**	NA	35	NA	NS	NA	**70**	NA	NA
Weight not given but assumed to be 70Kg. No need to estimate the amount of copper in water consumed as exposure estimates are provided in the article.									
37	79	30.9	42	NS	NS	NS	79	NA	NA
No need to estimate the amount of copper in water consumed as the exposure estimates are provided in article.									
42	0.1	**47**	210	NS	**257**	**152**	**0.222**	**15**	**31.08**
42	0.1	**47**	350	NS	**397**	**222**	**0.292**	**16**	**40.88**
Age estimated from Poiley (1972) based on specie, strain and body weight. Weight at midpoint estimated from Poiley (1972) based on specie, strain and age. Consumption of feed derived from the NAS (1972) and consumption of water derived from the CCAC (1984).									
43	7.4	28	28	16.7	56	42	**12.05**	70.91	NA

Weight at midpoint estimated from the reported weight at onset and termination. Average consumption reported in the study.									
44	**0.0374**	**21**	84	NS	**105**	**63**	**0.179**	**19**	**25.06**
Animals reported as being in the weaning stage. Estimate of 21 days for the age of weaning rats derived from the CCAC (1984). Weight at onset and midpoint estimated from Poiley (1972) based on specie, strain, sex and age. Consumption of feed derived from the NAS (1972) and consumption of water derived from the Canadian Council on Animal Care (CCAC) (1984).									
48	NS	**21**	7	NS	28	24.5	**0.069**	**9**	NA
48	NS	**21**	28	NS	49	35	**0.120**	**16**	NA
48	NS	**21**	56	NS	68	44.5	**0.191**	**19**	NA
48	NS	**21**	84	NS	105	63	**0.288**	**20**	NA
48	NS	**21**	112	NS	133	66.5	**0.304**	**20**	NA
Age at onset and mid-point estimated from Poiley (1972) based on specie, strain, sex and body weight. Consumption of feed derived from the NAS (1972).									
50	0.0107	21	28	NS	49	35	**0.022**	**3.3**	**3.3**
Body weight at midpoint estimated from Poiley (1972) based on specie, strain, sex and body weight. Feed consumption estimates derived from the Louisiana Veterinary Medical Association (LVMA) (2007).									
54	70	32	1	NA	35	35	**70**	NA	200
Body weight assumed to be 70kg.									
55	0.16	28	112	NS	140	56	**0.233**	**20**	**NA**
Body weight at onset and mid-point estimated from Poiley (1972) based on specie, strain, sex and body weight. Consumption of feed derived from the NAS (1972).									
56	0.125	**34**	252	0.372	**NA**	**NA**	**0.249**	**21**	**34.86**
Age at onset and mid-point estimated from Poiley (1972) based on specie, strain, sex and body weight. Consumption of feed derived from the NAS (1972) and consumption of water derived from the CCAC (1984).									
63	NS	**21**	NS	NS	NS	**70**	**70**	NA	NA
Weight assumed to be 70kg									
75	**0.139**	35	105	0.322	140	**87.5**	**0.231**	**29.5**	**86**
Body weight at onset and mid-point derived from Poiley (1972) based on specie, strain, sex and body weight. Consumption of feed derived from the NAS (1972) and consumption of water derived from the CCAC (1984).									
80	NS	70	42	NA	112	91	**0.250**	20	NA
Body weight estimated from Poiley (1972) based on specie, strain, sex and age. Consumption of feed derived from the NAS (1972).									

82	NS	NS	1095	NA	NS/NA	NS/NA	**70**	NA	NA
Body weight assumed to be 70 kg									
98	**0.256**	56	56	NS	112	84	**0.342**	**20**	**47.88**
Body weight estimated from Poiley (1972) based on specie, strain, sex and age. Consumption of feed derived from the NAS (1972) and consumption of water derived from the CCAC (1984).									
99	**0.1**	90	20	NS	110	100	**0.3**	**18**	**42**
Body weight estimated from Poiley (1972) based on specie, strain, sex and age. Consumption of feed derived from the NAS (1972) and consumption of water derived from the CCAC (1984).									
103	**0.0154**	30	906	NS	936	483	**0.035**	**5.25**	**5.25**
103	**0.0154**	30	776	NS	806	418	**0.034**	**5.1**	**5.1**
Body weight estimated from Poiley (1972) based on specie, strain, sex and age. Feed and water consumption estimates derived from the LVMA (2007).									
104	64	NA	77	NS	34	NA	64	NA	NA
Weight and age assumed to be constant from the beginning to the end of the study. Amount of copper consumed provided in the article.									
109	NS	NA	1	NA	NA	NA	**70**	NA	200
Weight assumed to be 70kg.									
110	NS	NA	1	NA	NA	NA	**70**	NA	200
Weight assumed to be 70kg.									
111	NS	NA	60	NA	NA	NA	**70**	NA	1500
Weight assumed to be 70kg.									
112	NA	37	60	NA	NA	NA	**70**	NA	1500
Weight assumed to be 70kg.									
114	4.99	17	70	NA	62	48	11.6	538.1	NA
117	0.09	**25**	120	NA	**145**	**85**	**0.300**	**20**	NA
Age at onset was estimated based on body weight from Poiley (1972), weight at midpoint estimated from Poiley (1972) and consumption of feed derived from the NAS (1972).									
126	21.25	NS	30	NS	NS	NS	29.74	610	NA
136	NS	70	133	NA	203	98	**26**	**3.9**	NA
Weight at midpoint estimated from Poiley (1972) and feed consumption estimated from the LVMA (2007).									
138	NS	32	42	NS	NA	NA	71	NA	NA

140	NS	NS	41	NS	NA	NA	**0.256**	**20**	**2.8**
Adult weight assumed to be 256g, feed consumption estimated from the NAS (1972) and water consumption estimated from the CCAC (1984).									
146	NS	38	18	NA	NA	NA	75	NA	NA
152	NA	56	84	NS	140	98	**3**	**110**	NA
Weight and feed consumption derived from the National Laboratory Animal Centre (NLAC) (2001)									
158	NS	60	84	NS	144	102	**25**	**3.75**	NA
Body weight estimated from Poiley (1972) and feed consumption estimated from LVMA (2007).									
172	6	18	10	NS	28	23	**6**	270	NA
Weight at midpoint assumed to be 6kg based on weight at onset and termination.									
178	0.18-0.25	50	20	NS	75	62.5	**0.285**	**20**	NA
Weight at midpoint estimated from Poiley (1972) and feed consumption derived from the NAS (1972).									
180	NS	120	60	NS	180	150	**0.44**	**20**	**61.6**
Weight at midpoint estimated from Poiley (1972). Feed consumption estimated from the NAS (1972). Water consumption estimated from the CCAC (1984).									
187	NS	28	7	NS	35	32	**0.075**	NA	**2.55**
Weight at midpoint estimated from Poiley (1972) and water consumption estimated from the CCAC (1984).									

Note. ID#, identification number corresponds with ref(ID#) in table A1; Exp, experiment number; Weight at T1, body weight at the beginning of the study; Age at T1, age at the Beginning of the study; Exposure T, exposure duration; Weight at T2, weight at the end of the study; Age at T2, age at the end of the study.

Table E2: Estimates and Assumptions for Copper Intake and Bodyweight – Copper Deficiency

ID #	*Weight at T1 (kg)*	*Age at T1 (days)*	*Exposure T (days)*	*Weight at T2*	*Age at T2*	*Age at Midpoint*	*Weight at Midpoint (kg)*	*Consumption Feed (g)*	*Consumption water (ml)*
1	NS	0	18	NS	18	**9**	**0.005**	**2.85**	**2.85**
Body weight estimated from Poiley (1972) based on specie, strain, sex and age. Feed and water consumption estimates derived from the LVMA (2007)									
4	**0.0374**	**21**	42	NS	**63**	**42**	**0.098**	**18**	**13.65**
Animals reported as being in the weaning stage. Estimate of 21 days for the age of a weaning rat derived from the CCAC (1984). Weight at midpoint estimated from Poiley (1972) based on specie, strain, sex and age. Consumption of feed derived from the NAS (1972) and consumption of water derived from the CCAC (1984).									
8	0.034	**168**	100	NS	**268**	**218**	**0.036**	**5.4**	**5.4**
Age at onset estimated from Poiley (1972) based on specie, strain, sex and body weight. Weight at mid-point estimated from Poliey (1972) based on specie, strain, sex and age.									
16	**0.0594**	**21**	28	NS	**49**	**35**	**0.13**	**17**	**18.2**
Animals reported as being in the weaning stage. Estimate of 21 days for the age of weaning rats derived from the NAS (1984). Weight at onset and midpoint estimated from Poiley (1972) based on specie, strain, sex and age. Consumption of feed based on NAS (1972) and consumption of water based on the CCAC (1984).									
17	**0.0594**	**21**	7	NS	**28**	**24.5**	**0.079**	**12**	**11.088**
17	**0.0594**	**21**	21	NS	**42**	**31.5**	**0.115**	**16**	**16.1**
17	**0.0594**	**21**	35	NS	**56**	**38.5**	**0.147**	**17**	**20.58**
Animals reported as being in the weaning stage. Estimate of 21 days for the age of weaning rats derived from the CCAC (1984). Weight at onset and midpoint estimated from Poiley (1972) based on specie, strain, sex and age. Consumption of feed derived from the NAS (1972) and consumption of water derived from the CCAC (1984).									
18	74	26	24	NS	NA	26	74	NA	NA
Weight and age is assumed to be constant from the beginning to the end of the experiment. Amount of copper consumed provided in the article.									
19	0.099	17.5	38.5	NS	56	36.75	**0.14**	**17**	**19.6**
Weight at mid-point estimated from Poiley (1972) based on specie, strain, sex and age. Consumption of feed derived from the NAS (1972) and consumption of water derived from the CCAC (1984).									
24	**0.0594**	**21**	35	NS	**56**	**38.5**	**0.147**	**17**	**20.58**
Animals reported as being in the weaning stage. Estimate of 21 days for the age of weaning rats derived from the CCAC (1984). Weight at onset and midpoint estimated from Poiley (1972) based on specie, strain, sex and age. Consumption of feed derived from the NAS (1972) and consumption of water derived from the CCAC (1984).									
27	**0.0436**	49	60	NS	109	79	**0.025**	**3.69**	**3.69**
Weight at onset and midpoint estimated from Poiley (1972) based on specie, strain, sex and age. Feed and water consumption estimates derived from the LVMA (2007).									
31	**70**	22-35	90	NS	22-35	22-35	70	NA	NA

Weight at onset assumed to be 70kg for adult male. Weight and age is assumed to be constant from the beginning to the end of the study. Amount of copper consumed provided in the article.									
32	**0.018**	**21**	140	NS	**161**	**91**	**0.373**	**20**	**52.178**
Animals reported as being in the weaning stage. Estimate of 21 days for the age of weaning rats derived from the CCAC (1984). Weight at onset and midpoint estimated from Poiley (1972) based on specie, strain, sex and age. Consumption of feed derived from the NAS (1972) and consumption of water derived from the CCAC (1984).									
33	0.046	**21**	63	NS	**84**	**52.5**	**0.216**	**21**	**30.24**
Animals reported as being in the weaning stage. Estimate of 21 days for the age of weaning rats derived from the CCAC (1984). Weight at midpoint estimated from Poiley (1972) based on specie, strain, sex and age. Consumption of feed derived from the NAS (1972) and consumption of water derived from the Canadian Council on Animal Care (CCAC) (1984).									
34	**0.057**	**21**	49	NS	**70**	**45.5**	**0.167**	**18**	**23.352**
Animals reported as being in the weaning stage. Estimate of 21 days for the age of weaning rats derived from the CCAC (1984). Weight at onset and midpoint estimated from Poiley (1972) based on specie, strain, sex and age. Consumption of feed derived from the NAS (1972) and consumption of water derived from the CCAC (1984).									
37	79	20-59	42	NS	NA	NA	79	NA	NA
Weight and age is assumed to be constant from the beginning to the end of the study. Amount of copper consumed provided in the article.									
38	**0.0533**	21	35	NS	56	38.5	**0.161**	**17**	**22.54**
38	NA	0	56	NS	56	28	**0.096**	**13.5**	**13.454**
Weight at onset and midpoint estimated from Poiley (1972) based on specie, strain, sex and age. Consumption of feed derived from the NAS (1972) and consumption of water derived from the CCAC (1984).									
39	6	21	77	46	98	**59.5**	**20**	**554**	NA
Weight at onset and termination given. Weight at midpoint estimated from Queensland Government 2005. Consumption of feed derived from Cromwell (1989).									
40	**0.057**	**21**	28	NS	49	**35**	**0.1326**	**16**	**18.564**
Animals reported as being in the weaning stage. Estimate of 21 days for the age of weaning rats derived from the CCAC (1984). Weight at midpoint estimated from Poiley (1972) based on specie, strain, sex and age. Consumption of feed derived from the NAS (1972) and consumption of water derived from the CCAC (1984).									
41	0.11	35	84	NS	119	77	**0.223**	**21**	**31.22**
Weight at midpoint estimated from Poiley (1972) based on specie, strain, sex and age. Consumption of feed derived from the NAS (1972) and consumption of water derived from the CCAC (1984).									
44	**0.0374**	**21**	84	NS	**105**	**63**	**0.179**	**19**	**25.06**
Animals reported as being in the weaning stage. Estimate of 21 days for the age of weaning rats derived from the CCAC (1984). Weight at onset and midpoint estimated from Poiley (1972) based on specie, strain, sex and age. Consumption of feed derived from the NAS (1972) and consumption of water derived from the CCAC (1984).									
45	**0.0374**	**21**	35	NS	**56**	**38.5**	**0.161**	**17**	**22.54**

Animals reported as being in the weaning stage. Estimate of 21 days for the age of weaning rats derived from the CCAC (1984). Weight at onset and midpoint estimated from Poiley (1972) based on specie, strain, sex and age. Consumption of feed derived from the NAS (1972) and consumption of water derived from the CCAC (1984).									
47	0.0425	**21**	28	NS	**49**	**35**	**0.127**	**15**	**17.71**
Animals reported as being in the weaning stage. Estimate of 21 days for the age of weaning rats derived from the CCAC (1984). Weight at onset and midpoint estimated from Poiley (1972) based on specie, strain, sex and age. Consumption of feed derived from the NAS (1972) and consumption of water derived from the CCAC (1984).									
50	0.01065	21	28	NS	49	35	**0.027**	**4.065**	**4.065**
Weight at midpoint estimated from Poiley (1872) based on specie, strain, sex and age. Feed and water consumption estimates derived from the LVMA (2007).									
51	**0.27**	**72**	28	NS	**100**	**86**	**0.304**	**18**	**42.56**
Animals reported as being adults. Estimate of 72 days for adult rats derived from the CCAC (1984). Weight at onset and midpoint estimated from Poiley (1972) based on specie, strain, sex and age.									
52	**0.238**	180	70	NS	250	215	**0.271**	10.1	**NA**
52	**0.325**	720	70	NS	790	755	**0.325**	13.7	**NA**
Weight at onset and midpoint estimated from Poiley (1972) based on specie, strain, sex and age. Amount of copper consumed provided in the article.									
53	**0.023**	10	60	NS	70	40	**0.108**	**15**	**15.12**
Weight at onset and midpoint estimated from Poiley (1972) based on specie, strain, sex and age. Consumption of feed derived from the NAS (1972) and consumption of water derived from the CCAC (1984).									
55	**0.0989**	28	112	NS	140	84	**0.358**	**20**	**50.12**
Weight at onset and midpoint estimated from Poiley (1972) based on specie, strain, sex and age. Consumption of feed derived from the NAS (1972) and consumption of water derived from the CCAC (1984).									
58	**0.0941**	21	98	NS	119	70	**0.02276**	**3.41**	**3.41**
Weight at onset and midpoint estimated from Poiley (1972) based on specie, strain, sex and age. Feed and water consumption derived from the LVMA (2007).									
62	**0.0575**	**21**	161	NS	**182**	**101.5**	**0.315**	**18**	**44.1**
Animals reported as being in the weaning stage. Estimate of 21 days for the age of weaning rats derived from the CCAC (1984). Weight at onset and midpoint estimated from Poiley (1972) based on specie, strain, sex and age. Consumption of feed derived from the NAS (1972) and consumption of water derived from the CCAC (1984).									
66	**0.0594**	21	35	NS	56	38.5	0.161	**18**	**22.54**
Weight at onset and midpoint estimated from Poiley (1972) based on specie, strain, sex and age. Consumption of feed derived from the NAS (1972) and consumption of water derived from the CCAC (1984).									
67	0.011	21	35	NS	56	**38.5**	**0.02**	**3**	**3**

Weight at midpoint estimated from Poiley (1972) based on specie, strain, sex and age. Feed and water consumption estimates derived from the LVMA (2007).									
68	**0.011**	21	21	NS	42	31.5	**0.01675**	**2.5**	**2.5**
Weight at onset and midpoint estimated from Poiley (1972) based on specie, strain, sex and age. Feed and water consumption estimates derived from the LVMA (2007).									
70	**0.01803**	**21**	35	NS	**56**	**38.5**	**0.161**	**17**	**22.54**
Animals reported as being in the weaning stage. Estimate of 21 days for the age of weaning rats derived from the CCAC (1984). Weight at onset and midpoint estimated from Poiley (1972) based on specie, strain, sex and age. Consumption of feed derived from the NAS (1972) and consumption of water derived from the CCAC (1984).									
71	70	NS	150	NS	NS	NS	70	NA	NA
Age assumed to be 70kg. Weight and age is assumed to be constant from the beginning to the end of the study. Amount of copper consumed provided in the article.									
72	0.05	**21**	28	NS	**49**	**35**	**0.133**	**16**	**18.62**
Animals reported as being in the weaning stage. Estimate of 21 days for the age of weaning rats derived from the CCAC (1984). Weight at onset and midpoint estimated from Poiley (1972) based on specie, strain, sex and age. Consumption of feed derived from the NAS (1972) and consumption of water derived from the CCAC (1984).									
73	**0.057**	**21**	28	NS	**49**	**35**	**0.133**	**16**	**18.62**
Animals reported as being in the weaning stage. Estimate of 21 days for the age of weaning rats derived from the CCAC (1984). Weight at onset and midpoint estimated from Poiley (1972) based on specie, strain, sex and age. Consumption of feed derived from the NAS (1972) and consumption of water derived from the CCAC (1984).									
74	**0.057**	**21**	28	NS	49	35	**0.133**	**16**	**18.62**
Weanling rats assumed to be 21 days of age (NAS 1969). Weight at onset and midpoint estimated from Poiley 1972. Feed consumption estimated from the NAS (1972) and water consumption estimated from CCAC (1984).									
76	**0.0178**	42	49	NS	91	66.5	**0.0221**	**3.32**	**3.32**
Weight at onset and midpoint estimated from Poiley (1972) based on specie, strain, sex and age. Feed and water consumption estimates derived from the LVMA (2007).									
77	**0.057**	21	77	NS	98	59.5	**0.249**	**19**	**34.86**
Weight at onset and midpoint estimated from Poiley (1972) based on specie, strain, sex and age. Consumption of feed derived from the NAS (1972) and consumption of water derived from the CCAC (1984).									
78	**0.04**	**21**	84	NS	105	63	**0.258**	**20**	**36.12**
Animals reported as being in the weaning stage. Estimate of 21 days for the age of weaning rats derived from the CCAC (1984). Weight at onset and midpoint estimated from Poiley (1972) based on specie, strain, sex and age. Consumption of feed derived from the NAS (1972) and consumption of water derived from the CCAC (1984).									
81	0.042	**21**	14	NS	**35**	**28**	**0.0985**	**14**	**13.79**
Animals reported as being in the weaning stage. Estimate of 21 days for the age of weaning rats derived from the CCAC (1984). Weight at onset and midpoint estimated from Poiley (1972) based on specie, strain, sex and age. Consumption of feed derived from the NAS (1972) and consumption of water derived from the CCAC (1984).									

83	**0.057**	**21**	21	NS	**42**	**31.5**	**0.116**	**15**	**16.24**
Animals reported as being in the weaning stage. Estimate of 21 days for the age of weaning rats derived from the CCAC (1984). Weight at onset and midpoint estimated from Poiley (1972) based on specie, strain, sex and age. Consumption of feed derived from the NAS (1972) and consumption of water derived from the CCAC (1984).									
84	**0.057**	**21**	30	NS	**51**	**36**	**0.137**	**18**	**19.18**
Animals reported as being in the weaning stage. Estimate of 21 days for the age of weaning rats derived from the CCAC (1984). Weight at onset and midpoint estimated from Poiley (1972) based on specie, strain, sex and age. Consumption of feed derived from the NAS (1972) and consumption of water derived from the CCAC (1984).									
85	**0.057**	21	35	NS	56	**56**	**0.233**	**20**	**32.62**
Animals reported as being in the weaning stage. Estimate of 21 days for the age of weaning rats derived from the CCAC (1984). Weight at onset and midpoint estimated from Poiley (1972) based on specie, strain, sex and age. Consumption of feed derived from the NAS (1972) and consumption of water derived from the CCAC (1984).									
86	**0.017**	7	28	NS	35	21	**0.058**	9	NA
Weight at onset and midpoint estimated from Poiley (1972) based on specie, strain, sex and age. Consumption of feed derived from the NAS (1972)									
89	0.06	**21**	42	NS	**63**	**42**	**0.181**	**19**	**25.34**
Animals reported as being in the weaning stage. Estimate of 21 days for the age of weaning rats derived from the CCAC (1984). Weight at onset and midpoint estimated from Poiley (1972) based on specie, strain, sex and age. Consumption of feed derived from the NAS (1972) and consumption of water derived from the CCAC (1984).									
90	**0.057**	**21**	35	NS	**106**	**63.5**	**0.268**	**20**	**37.52**
Animals reported as being in the weaning stage. Estimate of 21 days for the age of weaning rats derived from the CCAC (1984). Weight at onset and midpoint estimated from Poiley (1972) based on specie, strain, sex and age. Consumption of feed derived from the NAS (1972) and consumption of water derived from the CCAC (1984).									
91	NS	**21**	35	NS	56	45.5	**0.1807**	**19**	NA
Animals reported as being in the weaning stage. Estimate of 21 days for the age of weaning rats derived from the CCAC (1984). Weight at onset and midpoint estimated from Poiley (1972) based on specie, strain, sex and age. Consumption of feed derived from the NAS (1972).									
92	**0.129**	**40**	35	NS	**75**	**57.5**	**0.199**	**18**	**27.86**
Weight at onset and midpoint estimated from Poiley (1972) based on specie, strain, sex and age. Consumption of feed derived from the NAS (1972) and consumption of water derived from the CCAC (1984).									
95	**0.057**	21	24	NS	45	33	**0.1**	**15**	**14**
Weight at onset and midpoint estimated from Poiley (1972) based on specie, strain, sex and age. Consumption of feed derived from the NAS (1972) and consumption of water derived from the CCAC (1984).									
96	**0.057**	**21**	154	NS	**175**	**98**	**0.377**	**20**	**52.78**
Animals reported as being in the weaning stage. Estimate of 21 days for the age of weaning rats derived from the CCAC (1984). Weight at onset and midpoint estimated from Poiley (1972) based on specie, strain, sex and age. Consumption of feed derived from the NAS (1972) and consumption of water derived from the CCAC (1984).									
100	**0.0533**	**21**	42	NS	**63**	**42**	**0.181**	**19**	**25.34**

Animals reported as being in the weaning stage. Estimate of 21 days for the age of weaning rats derived from the CCAC (1984). Weight at onset and midpoint estimated from Poiley (1972) based on specie, strain, sex and age. Consumption of feed derived from the NAS (1972) and consumption of water derived from the CCAC (1984).									
102	70	**21-57**	77	NA	NA	NA	70	NA	NA
Age assumed to be 70kg. Weight and age is assumed to be constant from the beginning to the end of the study. Amount of copper consumed provided in the article.									
106	0.043	21	168	NS	189	105	**0.381**	**20**	**53.34**
Weight at onset and midpoint estimated from Poiley (1972) based on specie, strain, sex and age. Consumption of feed derived from the NAS (1972) and consumption of water derived from the CCAC (1984).									
107	0.054	28	42	NS	70	49	**0.175**	**19**	NA
Weight at midpoint estimated from Poiley (1972) and consumption estimated from NAS 1972.									
108	NS	49	49	NS	98	74	**0.250**	**20**	NA
Body weight estimated from Poiley (1972) and feed consumption estimated from the NAS 1972.									
115	NS	56	84	NS	140	126	**0.027**	**4.05**	NA
Weight at midpoint estimated from Poiley (1972) and feed consumption estimated from the LVMA (2007).									
118	NS	**21**	28	NS	**51**	**36**	**0.12**	**17**	NA
Animals reported as being in the weaning stage. Estimate of 21 days for the age of weaning rats derived from the CCAC (1984). Weight at midpoint estimated from Poiley (1972) based on specie, strain, sex and age. Consumption of feed derived from the NAS (1972).									
119	NS	**21**	30	NS	**51**	**36**	**0.120**	17.8	NA
Animals reported as being in the weaning stage. Estimate of 21 days for the age of weaning rats derived from the CCAC (1984). Weight at midpoint estimated from Poiley (1972) based on specie, strain, sex and age.									
120	NS	21	30	NS	51	36	**0.125**	**17**	NA
Weight at midpoint estimated from Poiley (1972) based on specie, strain, sex and age. Consumption of feed derived from the NAS (1972) estimates.									
121	NS	21	28	NS	52	37	**0.085**	**13**	NA
Weight at midpoint estimated from Poiley (1972) based on specie, strain, sex and age. Consumption of feed derived from the NAS (1972) estimates.									
122	NS	NA	42	NS	NA	NA	0.087	NA	NA
Information on copper intake and body weight provided in the article.									
123	NS	21	35	NS	56	38.5	**0.130**	**17**	NA
Weight at midpoint estimated from Poiley (1972) based on specie, strain, sex and age. Consumption of feed derived from the NAS (1972) estimates.									
125	0.25	56	180	NS	236	146	**0.440**	**20**	NA
Weight at midpoint estimated from Poiley (1972) based on specie, strain, sex and age. Consumption of feed derived from the NAS (1972).									

129	NS	NA	56	NA	NA	NA	78.4	NA	NA
Information on copper intake and body weight provided in the article.									
133	NS	21	42	NS	63	42	**0.167**	**18**	NA
133	NS	21	42	NS	63	42	**0.155**	**15**	NA
Weight at midpoint estimated from Poiley (1972) based on specie, strain, sex and age. Consumption of feed derived from the NAS (1972).									
137	NS	70	470	NS	540	305	**0.5**	**22**	NA
Weight at midpoint estimated from Poiley (1972) based on specie, strain, sex and age. Consumption of feed based on NAS (1972) estimates.									
141	NS	72	35	NS	113	93	**0.250**	**20**	**37.5**
141	NS	42	35	NS	87	65	**0.200**	**3**	**3**
Weight at midpoint estimated from Poiley (1972) based on specie, strain, sex and age. Consumption of feed for rats derived from the NAS (1972) estimates and water consumption based from CCAC 1984. Consumption of feed and water derived from the LVMA (2007).									
142	NS	**21**	35	NS	56	39	**0.125**	**16**	NA
Animals reported as being in the weaning stage. Estimate of 21 days for the age of weaning rats derived from the NAS (1969). Weight at midpoint estimated from Poiley (1972) based on specie, strain, sex and age. Consumption of feed derived from the NAS (1972) estimates.									
143	NS	**21**	35	NS	56	39	**0.125**	**16**	NA
Animals reported as being in the weaning stage. Estimate of 21 days for the age of weaning rats derived from the CCAC (1984). Weight at midpoint estimated from Poiley (1972) based on specie, strain, sex and age. Consumption of feed derived from the NAS (1972).									
144	NS	**21**	28	NS	49	35	**0.125**	**17**	NA
Animals reported as being in the weaning stage. Estimate of 21 days for the age of weaning rats derived from the CCAC (1984). Weight at midpoint estimated from Poiley (1972) based on specie, strain, sex and age. Consumption of feed derived from the NAS (1972).									
148	NS	28	60	NS	88	58	**0.232**	**21**	NA
Weight at midpoint estimated from Poiley (1972) based on specie, strain, sex and age. Consumption of feed based on NAS (1972) estimates.									
149	NS	21	35	NS	56	39	**0.155**	**17**	NA
Weight at midpoint estimated from Poiley (1972) based on specie, strain, sex and age. Consumption of feed derived from the NAS (1972) estimates.									
167	NS	**21**	35	NS	56	38.5	**0.1**	**15**	NA
Animals reported as being in the weaning stage. Estimate of 21 days for the age of weaning rats derived from the CCAC (1984). Weight at midpoint estimated from Poiley (1972) based on specie, strain, sex and age. Consumption of feed derived from the NAS (1972).									
177	NS	**21**	28	NS	**49**	**35**	**0.125**	**17**	NA
Animals reported as being in the weaning stage. Estimate of 21 days for the age of weaning rats derived from the CCAC (1984). Weight at midpoint estimated from Poiley (1972) based on specie, strain, sex and age. Consumption of feed derived from the NAS (1972).									
179	NS	**21**	28	NS	**49**	**35**	**0.125**	**16**	NA
Animals reported as being in the weaning stage. Estimate of 21 days for the age of weaning rats derived from the CCAC (1984). Weight at midpoint estimated from Poiley (1972)									

based on specie, strain, sex and age. Consumption of feed derived from the NAS (1972).									
183	NS	**21**	35	NS	**56**	**38.5**	**0.125**	**16**	NA
Animals reported as being in the weaning stage. Estimate of 21 days for the age of weaning rats taken from NAS (1969). Weight at midpoint estimated from Poiley (1972) based on specie, strain, sex and age. Consumption of feed based on NAS (1972) estimates.									
185	NS	24	35	NS	59	42	**0.152**	**17**	NA
Weight at midpoint estimated from Poiley (1972) based on specie, strain, sex and age. Consumption of feed derived from the NAS (1972).									
202	NS	21	19	NS	40	31	**0.125**	**17**	NA
202	NS	21	19	NS	40	31	**0.115**	**16**	NA
Weight at midpoint estimated from Poiley (1972) based on specie, strain, sex and age. Consumption of feed derived from the NAS (1972).									
211	NS	165	49	NS	214	190	**0.5**	**21**	NA
Weight at midpoint estimated from Poiley (1972) based on specie, strain, sex and age. Consumption of feed based on NAS (1972) estimates.									

Note. ID#, identification number corresponds with ref(ID#) in table A2; Exp, experiment number; Weight at T1, body weight at the beginning of the study; Age at T1, age at the beginning of the study; Exposure T, exposure duration; Weight at T2, weight at the end of the study; Age at T2, age at the end of the study.

TABLE E3: Final Estimates for 5 Dose Metrics – Copper Excess

ID#	*Exp*	*Grp*	*Base*	*Metric*	*Feed Consump. (kg)*	*Water Consump. (mL)*	*Mg/d*	*bw*	*bw $^{1/4}$*	*bw $^{2/3}$*	*bw $^{3/4}$*	*mg/bw*	*mg/bw$^{1/4}$*	*mg/bw$^{2/3}$*	*mg/ bw$^{3/4}$*
2	1	1	1.4	mg/d	NA	NA	1.4	82.2	0.4650	18.9052	27.2994	0.0170	0.4650	0.0741	0.0513
2	1	2	4.4	mg/d	NA	NA	4.4	82.2	1.4613	18.9052	27.2994	0.0535	1.4613	0.2327	0.1612
2	1	3	7.4	mg/d	NA	NA	7.4	82.2	2.4576	18.9052	27.2994	0.0900	2.4576	0.3914	0.2711
2	2	1	1.1	mg/d	NA	NA	1.1	61.3	0.3931	15.5468	21.9076	0.0179	0.3931	0.0708	0.0502
2	2	2	4.1	mg/d	NA	NA	4.1	61.3	1.4653	15.5468	21.9076	0.0669	1.4653	0.2637	0.1871
2	2	3	7.1	mg/d	NA	NA	7.1	61.3	2.5374	15.5468	21.9076	0.1158	2.5374	0.4567	0.3241
Habitual dietary Cu intake for males and females provided in the article (males =1.4 mg/day, females = 1.1 mg/day)															
6	1	1	1.25	mg/d	NA	NA	1.25	70	2.8925	16.9850	24.2005	0.0179	0.4322	0.0736	0.0517
6	1	2	6.25	mg/d	NA	NA	6.25	70	2.8925	16.9850	24.2005	0.1607	3.8894	0.6623	0.4649
Habitual dietary Cu estimated to be 1.25 mg/day (Baker 1999a)															
10	1	1	5.6	mg/kg f	0.018	NA	0.1008	0.165	0.6373	0.3008	0.2589	0.6109	0.1582	0.3351	0.3894
10	1	2	250	mg/kg f	0.018	NA	4.5	0.165	0.6373	0.3008	0.2589	27.2727	7.0606	14.9586	17.3820
Average levels of copper in feed assumed to be 5.6 mg/kg feed/day (NAS 1972)															
14	1	1	0	mg/d	NA	NA	1.4	70	2.8925	16.9850	24.2005	0.0200	0.4840	0.0824	0.0579
14	1	2	2	mg/d	NA	NA	3.4	70	2.8925	16.9850	24.2005	0.0486	1.1755	0.2002	0.1405
Habitual dietary Cu estimated to be 1.4mg/day (Baker 1999a)															
20	1	1	10	mg/kg	0.009	NA	0.09	0.0692	0.5129	0.1686	0.1350	1.3000	0.1755	0.5338	0.6668
20	1	2	3000	mg/kg	0.009	NA	27	0.0692	0.5129	0.1686	0.1350	390.0043	52.6369	160.1404	200.0521
20	1	3	4000	mg/kg	0.009	NA	36	0.0692	0.5129	0.1686	0.1350	520.0058	70.1825	213.5205	266.7361
20	1	4	5000	mg/kg	0.009	NA	45	0.0692	0.5129	0.1686	0.1350	650.0072	87.7281	266.9006	333.4201
20	1	5	6000	mg/kg	0.009	NA	54	0.0692	0.5129	0.1686	0.1350	780.0087	105.2738	320.2808	400.1041
20	2	1	10	mg/kg	0.012	NA	0.12	0.0799	0.5316	0.1854	0.1502	1.5026	0.2257	0.6471	0.7988
20	2	2	3000	mg/kg	0.012	NA	36	0.0799	0.5316	0.1854	0.1502	450.7889	67.7205	194.1257	239.6379
20	2	3	4000	mg/kg	0.012	NA	48	0.0799	0.5316	0.1854	0.1502	601.0518	90.2940	258.8342	319.5172
20	2	4	5000	mg/kg	0.012	NA	60	0.0799	0.5316	0.1854	0.1502	751.3148	112.8675	323.5428	399.3965
20	2	5	6000	mg/kg	0.012	NA	72	0.0799	0.5316	0.1854	0.1502	901.5778	135.4410	388.2513	479.2758

20	3	1	10	mg/kg	0.015	NA	0.15	0.0997	0.5619	0.2150	0.1774	1.5048	0.2670	0.6977	0.8455
20	3	2	3000	mg/kg	0.015	NA	45	0.0997	0.5619	0.2150	0.1774	451.4446	80.0867	209.3183	253.6626
20	3	3	4000	mg/kg	0.015	NA	60	0.0997	0.5619	0.2150	0.1774	601.9262	106.7823	279.0910	338.2168
20	3	4	5000	mg/kg	0.015	NA	75	0.0997	0.5619	0.2150	0.1774	752.4077	133.4779	348.8638	422.7711
20	3	5	6000	mg/kg	0.015	NA	90	0.0997	0.5619	0.2150	0.1774	902.8892	160.1734	418.6366	507.3253
20	4	1	10	mg/kg	0.016	NA	0.16	0.1195	0.5880	0.2426	0.2032	1.3389	0.2721	0.6595	0.7872
20	4	2	3000	mg/kg	0.016	NA	48	0.1195	0.5880	0.2426	0.2032	401.6736	81.6393	197.8469	236.1649
20	4	3	4000	mg/kg	0.016	NA	64	0.1195	0.5880	0.2426	0.2032	535.5649	108.8524	263.7959	314.8865
20	4	4	5000	mg/kg	0.016	NA	80	0.1195	0.5880	0.2426	0.2032	669.4561	136.0655	329.7449	393.6081
20	4	5	6000	mg/kg	0.016	NA	96	0.1195	0.5880	0.2426	0.2032	803.3473	163.2786	395.6938	472.3298
20	5	1	10	mg/kg	0.017	NA	0.17	0.1393	0.6109	0.2687	0.2280	1.2204	0.2783	0.6326	0.7456
20	5	2	3000	mg/kg	0.017	NA	51	0.1393	0.6109	0.2687	0.2280	366.1163	83.4800	189.7883	223.6695
20	5	3	4000	mg/kg	0.017	NA	68	0.1393	0.6109	0.2687	0.2280	488.1551	111.3067	253.0511	298.2260
20	5	4	5000	mg/kg	0.017	NA	85	0.1393	0.6109	0.2687	0.2280	610.1938	139.1333	316.3138	372.7826
20	5	5	6000	mg/kg	0.017	NA	102	0.1393	0.6109	0.2687	0.2280	732.2326	166.9600	379.5766	447.3391
20	6	1	10	mg/kg	0.018	NA	0.18	0.1592	0.6317	0.2937	0.2520	1.1307	0.2850	0.6128	0.7142
20	6	2	3000	mg/kg	0.018	NA	54	0.1592	0.6317	0.2937	0.2520	339.1960	85.4886	183.8365	214.2577
20	6	3	4000	mg/kg	0.018	NA	72	0.1592	0.6317	0.2937	0.2520	452.2613	113.9847	245.1153	285.6769
20	6	4	5000	mg/kg	0.018	NA	90	0.1592	0.6317	0.2937	0.2520	565.3266	142.4809	306.3941	357.0962
20	6	5	6000	mg/kg	0.018	NA	108	0.1592	0.6317	0.2937	0.2520	678.3920	170.9771	367.6730	428.5154
20	7	1	10	mg/kg	0.02	NA	0.2	0.3258	0.7555	0.4735	0.4312	0.6139	0.2647	0.4224	0.4638
20	7	2	3000	mg/kg	0.02	NA	60	0.3258	0.7555	0.4735	0.4312	184.1621	79.4170	126.7216	139.1355
20	7	3	4000	mg/kg	0.02	NA	80	0.3258	0.7555	0.4735	0.4312	245.5494	105.8893	168.9621	185.5140
20	7	4	5000	mg/kg	0.02	NA	100	0.3258	0.7555	0.4735	0.4312	306.9368	132.3617	211.2026	231.8925
20	7	5	6000	mg/kg	0.02	NA	120	0.3258	0.7555	0.4735	0.4312	368.3241	158.8340	253.4431	278.2710
22	1	1	5.6	mg/kg	0.009	NA	0.0504	0.06926	0.5130	0.1687	0.1350	0.7277	0.0982	0.2988	0.3733
22	1	2	2000	mg/kg	0.009	NA	18	0.06926	0.5130	0.1687	0.1350	259.8903	35.0875	106.7294	133.3247
22	2	1	5.6	mg/kg	0.012	NA	0.0672	0.07986	0.5316	0.1854	0.1502	0.8415	0.1264	0.3624	0.4473
22	2	2	2000	mg/kg	0.012	NA	24	0.07986	0.5316	0.1854	0.1502	300.5259	45.1470	129.4171	159.7586
22	3	1	5.6	mg/kg	0.015	NA	0.084	0.09968	0.5619	0.2150	0.1774	0.8427	0.1495	0.3907	0.4735
22	3	2	2000	mg/kg	0.015	NA	30	0.09968	0.5619	0.2150	0.1774	300.9631	53.3911	139.5455	169.1084
22	4	1	5.6	mg/kg	0.018	NA	0.1008	0.1195	0.5880	0.2426	0.2032	0.8435	0.1714	0.4155	0.4959
22	4	2	2000	mg/kg	0.018	NA	36	0.1195	0.5880	0.2426	0.2032	301.2552	61.2295	148.3852	177.1237

22	5	1	5.6	mg/kg	0.019	NA	0.1064	0.2128	0.6792	0.3564	0.3133	0.5000	0.1567	0.2985	0.3396
22	5	2	2000	mg/kg	0.019	NA	38	0.2128	0.6792	0.3564	0.3133	178.5714	55.9488	106.6111	121.2844
22	6	1	5.6	mg/kg	0.02	NA	0.112	0.3258	0.7555	0.4735	0.4312	0.3438	0.1482	0.2365	0.2597
22	6	2	2000	mg/kg	0.02	NA	40	0.3258	0.7555	0.4735	0.4312	122.7747	52.9447	84.4810	92.7570
Average levels of copper in feed assumed to be 5.6 mg/kg feed/day (NAS 1972)															
25	1	1	5.6	ppm	0.02	NA	0.112	0.312	0.7474	0.4600	0.4175	0.3590	0.1499	0.2435	0.2683
25	1	2	1505.6	ppm	0.02	NA	30.112	0.312	0.7474	0.4600	0.4175	96.5128	40.2903	65.4591	72.1313
25	2	1	5.6	ppm	0.016	NA	0.0896	0.211	0.6778	0.3544	0.3113	0.4246	0.1322	0.2528	0.2878
25	2	2	1505.6	ppm	0.016	NA	24.0896	0.211	0.6778	0.3544	0.3113	114.1687	35.5434	67.9685	77.3780
Average levels of copper in feed assumed to be 5.6 mg/kg feed/day (NAS 1972)															
26	1	1	0	ppm	NA	25.3	0.0003	0.181	0.6523	0.3200	0.2775	0.0014	0.0004	0.0008	0.0009
26	1	2	300	ppm	NA	25.3	7.6020	0.181	0.6523	0.3200	0.2775	42.0000	11.6549	23.7579	27.3949
26	1	3	1000	ppm	NA	25.3	25.3400	0.181	0.6523	0.3200	0.2775	140.0000	38.8496	79.1931	91.3162
26	1	4	3000	ppm	NA	25.3	76.0200	0.181	0.6523	0.3200	0.2775	420.0000	116.5489	237.5794	273.9485
26	1	5	10000	ppm	NA	25.3	253.4000	0.181	0.6523	0.3200	0.2775	1400.00	388.4964	791.9314	913.1617
26	1	6	30000	ppm	NA	25.3	760.2000	0.181	0.6523	0.3200	0.2775	4200.0000	1165.4891	2375.7942	2739.4850
26	2	1	0	ppm	NA	3.75	0.0001	0.025	0.3976	0.0855	0.0629	0.0015	0.0001	0.0004	0.0006
26	2	2	300	ppm	NA	3.75	1.125	0.025	0.3976	0.0855	0.0629	45.0000	2.8292	13.1581	17.8936
26	2	3	1000	ppm	NA	3.75	3.75	0.025	0.3976	0.0855	0.0629	150.0000	9.4308	43.8603	59.6453
26	2	4	3000	ppm	NA	3.75	11.25	0.025	0.3976	0.0855	0.0629	450.0000	28.2923	131.5808	178.9359
26	2	5	10000	ppm	NA	3.75	37.5	0.025	0.3976	0.0855	0.0629	1500.0000	94.3075	438.6027	596.4530
26	2	6	30000	ppm	NA	3.75	112.5	0.025	0.3976	0.0855	0.0629	4500.0000	282.9225	1315.8080	1789.3491
26	3	1	0	ppm	NA	17.5	0.0031	0.125	0.5946	0.2500	0.2102	0.0248	0.0052	0.0124	0.0147
26	3	2	300	ppm	NA	17.5	5.25	0.125	0.5946	0.2500	0.2102	42.0000	8.8294	21.0000	24.9733
26	3	3	1000	ppm	NA	17.5	17.5	0.125	0.5946	0.2500	0.2102	140.0000	29.4314	70.0000	83.2445
26	3	4	3000	ppm	NA	17.5	52.5	0.125	0.5946	0.2500	0.2102	420.0000	88.2941	210.0000	249.73335
26	3	5	10000	ppm	NA	17.5	175	0.125	0.5946	0.2500	0.2102	1400.0000	294.3137	700.0000	832.4450
26	3	6	30000	ppm	NA	17.5	525	0.125	0.5946	0.2500	0.2102	4200.0000	882.9412	2100.0000	2497.3349
26	4	1	0	ppm	NA	3.6	0.00004	0.024	0.3936	0.0832	0.0610	0.0015	0.0001	0.0004	0.0006
26	4	2	300	ppm	NA	3.6	1.08	0.024	0.3936	0.0832	0.0610	45.0000	2.7439	12.9802	17.7119
26	4	3	1000	ppm	NA	3.6	3.6	0.024	0.3936	0.0832	0.0610	150.0000	9.1464	43.2675	59.0397
26	4	4	3000	ppm	NA	3.6	10.8	0.024	0.3936	0.0832	0.0610	450.0000	27.4392	129.8025	177.1191

26	4	5	10000	ppm	NA	3.6	36	0.024	0.3936	0.0832	0.0610	1500.0000	91.4639	432.6749	590.3969
26	4	6	30000	ppm	NA	3.6	108	0.024	0.3936	0.0832	0.0610	4500.0000	274.2917	1298.0246	1771.1907
26	5	1	0	ppm	NA	NA	0.2431	0.154	0.6264	0.2873	0.2458	1.5786	0.3881	0.8461	0.9889
26	5	2	1000	ppm	NA	NA	13.156	0.154	0.6264	0.2873	0.2458	85.4286	21.0012	45.7906	53.5160
26	5	3	2000	ppm	NA	NA	25.74	0.154	0.6264	0.2873	0.2458	167.1429	41.0893	89.5904	104.7051
26	5	4	4000	ppm	NA	NA	51.909	0.154	0.6264	0.2873	0.2458	337.0714	82.8633	180.6739	211.1554
26	5	5	8000	ppm	NA	NA	111.111	0.154	0.6264	0.2873	0.2458	721.5000	177.3687	386.7318	451.9772
26	5	6	16000	ppm	NA	NA	182.325	0.154	0.6264	0.2873	0.2458	1183.9286	291.0490	634.5985	741.6614
26	6	1	0	ppm	NA	NA	0.150865	0.12	0.5886	0.2433	0.2039	1.2572	0.2563	0.6201	0.7400
26	6	2	1000	ppm	NA	NA	9.706	0.12	0.5886	0.2433	0.2039	80.8833	16.4909	39.8951	47.6052
26	6	3	2000	ppm	NA	NA	18.99	0.12	0.5886	0.2433	0.2039	158.2500	32.2649	78.0556	93.1406
26	6	4	4000	ppm	NA	NA	38.2965	0.12	0.5886	0.2433	0.2039	319.1375	65.0674	157.4122	187.8335
26	6	5	8000	ppm	NA	NA	81.9735	0.12	0.5886	0.2433	0.2039	683.1125	139.2766	336.9401	402.0569
26	6	6	16000	ppm	NA	NA	134.5125	0.12	0.5886	0.2433	0.2039	1120.9375	228.5427	552.8939	659.7459
26	7	1	0	ppm	NA	NA	0.03588	0.023	0.3894	0.0809	0.0591	1.5600	0.0921	0.4436	0.6075
26	7	2	1000	ppm	NA	NA	3.864	0.023	0.3894	0.0809	0.0591	168.0000	9.9221	47.7770	65.4246
26	7	3	2000	ppm	NA	NA	8.326	0.023	0.3894	0.0809	0.0591	362.0000	21.3798	102.9480	140.9745
26	7	4	4000	ppm	NA	NA	17.779	0.023	0.3894	0.0809	0.0591	773.0000	45.6536	219.8309	301.0312
26	7	5	8000	ppm	NA	NA	26.542	0.023	0.3894	0.0809	0.0591	1154.0000	68.1556	328.1822	449.4049
26	7	6	16000	ppm	NA	NA	64.791	0.023	0.3894	0.0809	0.0591	2817.0000	166.3730	801.1173	1097.0308
26	8	1	0	ppm	NA	NA	0.04416	0.022	0.3851	0.0785	0.0571	2.0073	0.1147	0.5624	0.7731
26	8	2	1000	ppm	NA	NA	3.864	0.022	0.3851	0.0785	0.0571	175.6364	10.0330	49.2140	67.6426
26	8	3	2000	ppm	NA	NA	8.326	0.022	0.3851	0.0785	0.0571	378.4545	21.6188	106.0445	145.7536
26	8	4	4000	ppm	NA	NA	17.779	0.022	0.3851	0.0785	0.0571	808.1364	46.1638	226.4430	311.2364
26	8	5	8000	ppm	NA	NA	26.542	0.022	0.3851	0.0785	0.0571	1206.4545	68.9173	338.0533	464.6400
26	8	6	16000	ppm	NA	NA	64.791	0.022	0.3851	0.0785	0.0571	2945.0455	168.2322	825.2133	1134.2210
26	9	1	0	ppm	NA	NA	0.103	0.335	0.7608	0.4824	0.4403	0.3075	0.1354	0.2135	0.2339
26	9	2	500	ppm	NA	NA	10.3	0.335	0.7608	0.4824	0.4403	30.7463	13.5387	21.3537	23.3913
26	9	3	1000	ppm	NA	NA	18.952	0.335	0.7608	0.4824	0.4403	56.5731	24.9112	39.2909	43.0399
26	9	4	2000	ppm	NA	NA	37.08	0.335	0.7608	0.4824	0.4403	110.6866	48.7392	76.8735	84.2085
26	9	5	4000	ppm	NA	NA	74.778	0.335	0.7608	0.4824	0.4403	223.2179	98.2907	155.0282	169.8205
26	9	6	8000	ppm	NA	NA	160.062	0.335	0.7608	0.4824	0.4403	477.7970	210.3909	331.8372	363.5002
26	10	1	0	ppm	NA	NA	0.11169	0.24	0.6999	0.3862	0.3429	0.4654	0.1596	0.2892	0.3257

26	10	2	500	ppm	NA	NA	7.65	0.24	0.6999	0.3862	0.3429	31.8750	10.9297	19.8086	22.3102
26	10	3	1000	ppm	NA	NA	14.076	0.24	0.6999	0.3862	0.3429	58.6500	20.1107	36.4478	41.0507
26	10	4	2000	ppm	NA	NA	27.54	0.24	0.6999	0.3862	0.3429	114.7500	39.3470	71.3110	80.3166
26	10	5	4000	ppm	NA	NA	55.539	0.24	0.6999	0.3862	0.3429	231.4125	79.3497	143.8105	161.9719
26	10	6	8000	ppm	NA	NA	118.881	0.24	0.6999	0.3862	0.3429	495.3375	169.8477	307.8258	346.7001
26	11	1	0	ppm	NA	NA	0.0318	0.03	0.4162	0.0965	0.0721	1.0600	0.0764	0.3294	0.4411
26	11	2	1000	ppm	NA	NA	5.04	0.03	0.4162	0.0965	0.0721	168.0000	12.1102	52.2015	69.9181
26	11	3	2000	ppm	NA	NA	10.86	0.03	0.4162	0.0965	0.0721	362.0000	26.0945	112.4818	150.6569
26	11	4	4000	ppm	NA	NA	23.19	0.03	0.4162	0.0965	0.0721	773.0000	55.7212	240.1891	321.7065
26	11	5	8000	ppm	NA	NA	34.62	0.03	0.4162	0.0965	0.0721	1154.0000	83.1853	358.5746	480.2707
26	11	6	16000	ppm	NA	NA	84.51	0.03	0.4162	0.0965	0.0721	2817.0000	203.0616	875.3074	1172.3767
26	12	1	0	ppm	NA	NA	0.03321	0.026	0.4016	0.0878	0.0647	1.2773	0.0827	0.3784	0.5129
26	12	2	1000	ppm	NA	NA	4.536	0.026	0.4016	0.0878	0.0647	174.4615	11.2961	51.6842	70.0556
26	12	3	2000	ppm	NA	NA	9.774	0.026	0.4016	0.0878	0.0647	375.9231	24.3405	111.3671	150.9532
26	12	4	4000	ppm	NA	NA	20.871	0.026	0.4016	0.0878	0.0647	802.7308	51.9756	237.8087	322.3393
26	12	5	8000	ppm	NA	NA	31.158	0.026	0.4016	0.0878	0.0647	1198.3846	77.5937	355.0210	481.2154
26	12	6	16000	ppm	NA	NA	76.059	0.026	0.4016	0.0878	0.0647	2925.3462	189.4119	866.6326	1174.6828
Background levels of copper in drinking water assumed to be 0.01 mg/L (Araya, 2004).															
35	1	1	0	mg/L	NA	200	0.002	70	2.8925	16.9850	24.2005	0.0001	0.0007	0.0001	0.0001
35	1	2	2	mg/L	NA	200	0.4	70	2.8925	16.9850	24.2005	0.0057	0.1383	0.0236	0.0165
35	1	3	4	mg/L	NA	200	0.8	70	2.8925	16.9850	24.2005	0.0114	0.2766	0.0471	0.0331
35	1	4	6	mg/L	NA	200	1.2	70	2.8925	16.9850	24.2005	0.0171	0.4149	0.0707	0.0496
35	1	5	8	mg/L	NA	200	1.6	70	2.8925	16.9850	24.2005	0.0229	0.5532	0.0942	0.061
Background levels of copper in drinking water assumed to be 0.01 mg/L (Araya, 2004).															
37	1	1	1.6	mg/day	NA	NA	1.6	79	2.9813	18.4113	1.4226	0.0203	0.5367	0.0869	1.4226
37	1	2	6	mg/day	NA	NA	6	79	2.9813	18.4113	3.8337	0.0759	2.0125	0.3259	3.8337
42	1	1	5	ppm	0.015	NA	0.075	0.222	0.6864	0.3666	0.3234	0.3378	0.1093	0.2046	0.2319
42	1	2	200	ppm	0.015	NA	3	0.222	0.6864	0.3666	0.3234	13.5135	4.3705	8.1825	9.2759
42	2	1	5	ppm	0.016	NA	0.08	0.292	0.7351	0.4401	0.3972	0.2740	0.1088	0.1818	0.2014
42	2	2	200	ppm	0.016	NA	3.2	0.292	0.7351	0.4401	0.3972	10.9589	4.3532	7.2705	8.0559

43	1	1	30	ppm	0.554	NA	16.62	12.05	1.8631	5.2560	6.4676	1.3793	8.9204	3.1621	2.5697
43	1	2	155	ppm	0.554	NA	85.87	12.05	1.8631	5.2560	6.4676	7.1261	46.0887	16.3374	13.2770
43	1	3	280	ppm	0.554	NA	155.12	12.05	1.8631	5.2560	6.4676	12.8730	83.2571	29.5128	23.9843
43	2	1	30	ppm	0.554	NA	16.62	12.05	1.8631	5.2560	6.4676	1.3793	8.9204	3.1621	2.5697
43	2	2	155	ppm	0.554	NA	85.87	12.05	1.8631	5.2560	6.4676	7.1261	46.0887	16.3374	13.2770
43	2	3	280	ppm	0.554	NA	155.12	12.05	1.8631	5.2560	6.4676	12.8730	83.2571	29.5128	23.9843
44	1	1	6	mg/kg f	0.021	NA	0.126	0.264	0.7168	0.4115	0.3683	0.4773	0.1758	0.3062	0.3421
44	1	2	250	mg/kg f	0.021	NA	5.25	0.264	0.7168	0.4115	0.3683	19.8864	7.3242	12.7572	14.2546
48	1	1	20	ppm	0.009	NA	0.18	0.06926	0.5130	0.1687	0.1350	2.5989	0.3509	1.0673	1.3332
48	1	2	1500	ppm	0.009	NA	13.5	0.06926	0.5130	0.1687	0.1350	194.9177	26.3156	80.0471	99.9935
48	2	1	20	ppm	0.016	NA	0.32	0.1195	0.5880	0.2426	0.2032	2.6778	0.5443	1.3190	1.5744
48	2	2	1500	ppm	0.016	NA	24	0.1195	0.5880	0.2426	0.2032	200.8368	40.8196	98.9235	118.0824
48	3	1	20	ppm	0.019	NA	0.38	0.191	0.6611	0.3317	0.2889	1.9895	0.5748	1.1458	1.3153
48	3	2	1500	ppm	0.019	NA	28.5	0.191	0.6611	0.3317	0.2889	149.2147	43.1108	85.9322	98.6438
48	4	1	20	ppm	0.02	NA	0.4	0.2882	0.7327	0.4363	0.3933	1.3879	0.5459	0.9168	1.0169
48	4	2	1500	ppm	0.02	NA	30	0.2882	0.7327	0.4363	0.3933	104.0944	40.9447	68.7583	76.2695
48	5	1	20	ppm	0.02	NA	0.4	0.3044	0.7428	0.4525	0.4098	1.3141	0.5385	0.8840	0.9761
48	5	2	1500	ppm	0.02	NA	30	0.3044	0.7428	0.4525	0.4098	98.5545	40.3887	66.2966	73.2045
50	1	1	498	ppm	0.0033	NA	1.6434	0.022	0.3851	0.0785	0.0571	74.7000	4.2671	20.9312	28.7691
50	1	2	200	ppm	0.0033	NA	0.66	0.249	0.7064	0.3958	0.3525	2.6506	0.9343	1.6675	1.8724
54	1	1	10	mg/L	NA	200	2	70	2.8925	16.9850	24.2005	0.0286	0.6914	0.2278	0.0826
55	1	1	25	ppm	0.02	NA	0.5	0.2326	0.6945	0.3782	0.3349	2.1496	0.7200	1.3220	1.4928
55	1	2	100	ppm	0.02	NA	2	0.2326	0.6945	0.3782	0.3349	8.5985	2.8799	5.2880	5.9714
56	1	1	0	mg/L	0.021	52.5	0.0005	0.375	0.7825	0.5200	0.4792	0.0014	0.0007	0.0010	0.0011
56	1	2	1250	mg/L	0.021	52.5	65.63	0.375	0.7825	0.5200	0.4792	175.0133	83.8677	126.2065	136.9553
Background levels of copper in drinking water assumed to be 0.01 mg/L (Araya, 2004).															
63	1	1	250	g/day	NS	NA	250000	70	2.8925	16.9850	24.2005	3571.4286	86430.1962	14718.8761	10330.3843

75	1	1	18	mg/kg f	0.0281	NA	0.5058	0.231	0.6933	0.3765	0.3332	2.1896	0.7296	1.3435	1.5180
75	1	2	100	mg/kg f	0.031	NA	3.1	0.231	0.6933	0.3765	0.3332	13.4199	4.4716	8.2342	9.3036
80	1	1	10	mg/kg	0.02	NA	0.2	0.2497	0.7069	0.3965	0.3532	0.8010	0.2829	0.5044	0.5662
80	1	2	1500	mg/kg	0.02	NA	30	0.2497	0.7069	0.3965	0.3532	120.1442	42.4391	75.6558	84.9293
82	1	1	45	mg/day	NA	NA	45	70	2.8925	16.9850	24.2005	0.6429	15.5574	2.6494	2.8925
98	1	1	5.6	mg/kg f	0.02	NA	0.112	0.342	0.7647	0.4890	0.4472	0.3275	0.1465	0.2290	0.2504
98	1	2	500	mg/kg f	0.02	NA	171	0.342	0.7647	0.4890	0.4472	500.00	223.6092	349.6595	382.3636
Average levels of copper in feed assumed to be 5.6 mg/kg feed/day (NAS 1972)															
99	1	1	5.6	mg/kg	0.018	NA	0.1008	0.3	0.7401	0.4481	0.4054	0.3360	0.1362	0.2249	0.2487
99	1	2	100	mg/kg	0.018	NA	31.68	0.3	0.7401	0.4481	0.4054	105.6000	42.8060	70.6921	78.1527
Average levels of copper in feed assumed to be 5.6 mg/kg feed/day (NAS 1972)															
103	1	1	0	ppm	0.0052	4	0.0001	0.035	0.4325	0.1070	0.0809	0.0011	0.0001	0.0004	0.0005
103	1	2	317	ppm	0.0052	4	1.2680	0.035	0.4325	0.1070	0.0809	36.2286	2.9316	11.8506	15.6700
Background levels of copper in drinking water assumed to be 0.01 mg/L (Araya, 2004).															
104	1	1	0	mg/l	NA	1.64	0.0164	64	2.8284	16.0000	22.6274	0.0003	0.0058	0.0010	0.0007
104	1	2	1	mg/l	NA	1.64	1.64	64	2.8284	16.0000	22.6274	0.0256	0.5798	0.1025	0.725
104	1	3	3	mg/l	NA	1.64	4.92	64	2.8284	16.0000	22.6274	0.0769	1.7395	0.3075	0.2174
104	1	4	5	mg/l	NA	1.64	8.2	64	2.8284	16.0000	22.6274	0.1281	2.8991	0.5125	0.3624
Background levels of copper in drinking water assumed to be 0.01 mg/L (Araya, 2004).															
109	1	1	0	mg/l	NA	200	0.002	70	2.8925	16.9850	24.2005	0.0001	0.0007	0.0001	0.0001
109	1	2	10	mg/l	NA	200	2	70	2.8925	16.9850	24.2005	0.0286	0.6914	0.1178	0.0826
Background levels of copper in drinking water assumed to be 0.01 mg/L (Araya, 2004).															
110	1	1	0	mg/l	NA	200	0.002	70	2.8925	16.9850	24.2005	0.0003	0.0007	0.0001	0.0008
110	1	2	2	mg/l	NA	200	0.4	70	2.8925	16.9850	24.2005	0.0057	0.1383	0.0236	0.0165
110	1	3	4	mg/l	NA	200	0.8	70	2.8925	16.9850	24.2005	0.0114	0.2766	0.0471	0.0331
110	1	4	6	mg/l	NA	200	1.2	70	2.8925	16.9850	24.2005	0.0171	0.4149	0.0707	0.0496

110	1	5	8	mg/l	NA	200	1.6	70	2.8925	16.9850	24.2005	0.0229	0.5532	0.0942	0.0661
Background levels of copper in drinking water assumed to be 0.01 mg/L (Araya, 2004).															
111	1	1	0.01	mg/l	NA	1500	0.015	70	2.8925	16.9850	24.2005	0.0002	0.0052	0.0009	0.0006
111	1	2	2	mg/l	NA	1500	3	70	2.8925	16.9850	24.2005	0.0429	1.0372	0.1766	0.1240
111	1	3	4	mg/l	NA	1500	6	70	2.8925	16.9850	24.2005	0.0857	2.0743	0.3533	0.2479
111	1	4	6	mg/l	NA	1500	9	70	2.8925	16.9850	24.2005	0.1286	3.1115	0.5299	0.3719
Background levels of copper in drinking water assumed to be 0.01 mg/L (Araya, 2004).															
112	1	1	0	mg/l	NA	1500	0.015	70	2.8925	16.9850	24.2005	0.0002	0.0052	0.0009	0.0006
112	1	2	2	mg/l	NA	1500	3	70	2.8925	16.9850	24.2005	0.0429	1.0372	0.1766	0.1240
112	1	3	4	mg/l	NA	1500	6	70	2.8925	16.9850	24.2005	0.0857	2.0743	0.3533	0.2479
112	1	4	5	mg/l	NA	1500	7.5	70	2.8925	16.9850	24.2005	0.1071	2.5929	0.4416	0.3099
Background levels of copper in drinking water assumed to be 0.01 mg/L (Araya, 2004).															
114	1	1	10	ppm	0.5381	NS	5.38	11.6	1.8455	5.1243	6.2856	0.4638	2.9152	1.0499	0.8559
114	1	2	135	ppm	0.5381	NS	72.64	11.6	1.8455	5.1243	6.2856	6.2621	39.3606	14.1755	11.5567
114	1	3	260	ppm	0.5381	NS	139.91	11.6	1.8455	5.1243	6.2856	12.0612	75.8114	27.3030	22.2590
114	2	1	15	ppm	0.5381	NS	8.07	11.6	1.8455	5.1243	6.2856	0.6957	4.3728	1.5748	1.2839
114	2	2	46	ppm	0.5381	NS	24.75	11.6	1.8455	5.1243	6.2856	2.1336	13.4110	4.8299	3.9376
114	2	3	77	ppm	0.5381	NS	41.43	11.6	1.8455	5.1243	6.2856	3.5716	22.4492	8.0849	6.5913
114	2	4	140	ppm	0.5381	NS	75.33	11.6	1.8455	5.1243	6.2856	6.4940	40.8182	14.7004	11.9846
117	1	1	10	ppm	0.02	NA	0.2	0.3	0.7401	0.4481	0.4054	0.6667	0.2702	0.4463	0.4934
117	1	2	1200	ppm	0.02	NA	24	0.3	0.7401	0.4481	0.4054	80	32.4288	53.5546	59.2066
126	1	1	12.4	mg/kg	0.61	NA	7.56	29.74	2.3353	9.5990	12.7352	0.2542	3.2373	0.7876	0.5936
126	1	2	250	mg/kg	0.61	NA	160.06	29.74	2.3353	9.5990	12.7352	5.3820	68.5405	16.6746	12.5683
126	2	1	12.4	mg/kg	0.61	NA	7.56	29.74	2.3353	9.5990	12.7352	0.2542	3.2373	0.7876	0.5936
126	2	2	50	mg/kg	0.61	NA	38.06	29.74	2.3353	9.5990	12.7352	1.2798	16.2980	3.9650	2.9886
126	2	3	100	mg/kg	0.61	NA	68.56	29.74	2.3353	9.5990	12.7352	2.3053	29.3586	7.1424	5.3835
136	1	1	0	mg/L	0.0039	3.9	0.00004	0.026	0.4016	0.0878	0.0647	0.0015	0.0001	0.0004	0.0006
136	1	2	120	mg/L	0.0039	3.9	0.468	0.026	0.4016	0.0878	0.0647	18.0000	1.1655	5.3325	7.2280

136	1	3	300	mg/L	0.0039	3.9	1.17	0.026	0.4016	0.0878	0.0647	45.0000	2.9137	13.3312	18.0699
Background levels of copper in drinking water assumed to be 0.01 mg/L (Araya, 2004).															
138	1	1	1.23	mg/d	NA	NA	1.23	71	2.9028	17.1464	24.4593	0.0173	0.4237	0.0717	0.0503
138	1	2	4.23	mg/d	NA	NA	4.23	71	2.9028	17.1464	24.4593	0.0596	1.4572	0.2467	0.1729
138	2	1	1.23	mg/d	NA	NA	1.23	71	2.9028	17.1464	24.4593	0.0173	0.4237	0.0717	0.0503
138	2	2	4.23	mg/d	NA	NA	4.23	71	2.9028	17.1464	24.4593	0.0596	1.4572	0.2467	0.1729
138	3	1	1.23	mg/d	NA	NA	1.23	71	2.9028	17.1464	24.4593	0.0173	0.4237	0.0717	0.0503
138	3	2	7.23	mg/d	NA	NA	7.23	71	2.9028	17.1464	24.4593	0.1018	2.4907	0.4217	0.2956
Habitual dietary Cu intake for males and females provided in the article (males =1.4 mg/day, females = 1.1 mg/day)															
140	1	1	0	µg/mL	0.02	35.8	0.0004	0.256	0.7113	0.4032	0.3599	0.0014	0.0005	0.0009	0.0010
140	1	2	250	µg/mL	0.02	35.8	8.95	0.256	0.7113	0.4032	0.3599	34.9609	12.5824	22.1988	24.8681
Background levels of copper in drinking water assumed to be 0.01 mg/L (Araya, 2004).															
146	1	1	7.8	mg/d	NA	NA	7.8	75	2.9428	17.7845	25.4857	0.104	2.6505	0.4386	0.3061
152	1	1	3.7	mg/d	0.11	NA	3.7	3	1.3161	2.0801	2.2795	1.2333	2.8114	1.7788	1.6232
152	1	2	350	mg/d	0.11	NA	350	3	1.3161	2.0801	2.2795	116.6667	265.9425	168.2624	153.5420
158	1	1	0	ppm	0.00375	NA	0.00001	0.025	0.3976	0.0855	0.0629	0.0015	0.0001	0.0004	0.0006
158	1	2	2	ppm	0.00375	NA	0.0075	0.025	0.3976	0.0855	0.0629	0.3	0.0189	0.0877	0.1193
Background levels of copper in drinking water assumed to be 0.01 mg/L (Araya, 2004).															
172	1	1	20	ppm	0.27	NA	5.4	6	1.5651	3.3019	3.8337	0.9000	3.4503	1.6354	1.4086
172	1	2	195	ppm	0.27	NA	52.65	6	1.5651	3.3019	3.8337	8.7750	33.6404	15.9452	13.7336
178	1	1	0	mg/d	0.02	39.9	0.0004	0.285	0.7307	0.4331	0.3901	0.0014	0.0005	0.0009	0.0010
178	1	2	12.12	mg/d	0.02	39.9	12	0.285	0.7307	0.4331	0.3901	42.1053	16.4237	27.7088	30.7643
Background levels of copper in drinking water assumed to be 0.01 mg/L (Araya, 2004).															
180	1	1	0	mg/l	0.02	61.6	0.0006	0.44	0.8144	0.5785	0.5402	0.0014	0.0008	0.0011	0.0011
180	1	2	100	mg/l	0.02	61.6	6.16	0.44	0.8144	0.5785	0.5402	14	7.5634	10.6483	11.4023
180	1	3	400	mg/l	0.02	61.6	24.64	0.44	0.8144	0.5785	0.5402	56.0000	30.2536	42.5931	45.6091
Background levels of copper in drinking water assumed to be 0.01 mg/L (Araya, 2004).															

187	1	1	0	µg/mL	NA	14	0.0001	0.075	0.5233	0.1778	25.4857	0.0019	0.0003	0.0008	0.00001
187	1	2	50	µg/mL	NA	14	0.7	0.075	0.5233	0.1778	25.4857	9.3333	1.3376	3.9360	0.0275
187	1	3	100	µg/mL	NA	14	1.4	0.075	0.5233	0.1778	25.4857	18.6667	2.6752	7.8720	0.0549
187	1	4	200	µg/mL	NA	14	2.8	0.075	0.5233	0.1778	25.4857	37.3333	5.3505	15.7441	0.1099
Background levels of copper in drinking water assumed to be 0.01 mg/L (Araya, 2004).															

Note. ID #, reference identification number corresponds with table A1; Exp, experiment number within the publication; Grp, group number within experiment; Base, reported dose of copper; Feed Consump., feed consumption; Water consump., water consumption; mg/bw, milligrams copper per kilogram body weight; $mg/bw^{1/4}$, milligrams copper per kilogram body $weight^{1/4}$; $mg/bw^{2/3}$, milligrams copper per kilogram $bodyweight^{2/3}$; $mg/bw^{3/4}$, milligrams copper per kilogram $bodyweight^{3/4}$, BW, body weight; Cu, copper; mg/kg f, milligrams of copper per kilogram of feed; mg/d, milligrams of copper per day; ppm, parts per million; mg/kg bw/day, milligrams of copper per kilogram body weight per day; mg/L, milligrams of copper per liter of water.

Table E4: Final Estimates for 5 Dose Metrics – Copper Deficiency

Ref	*Exp*	*Grp*	*Base*	*Metric*	*Food Consump. (kg)*	*Water Consump. (mL)*	*Mg/d*	*bw*	*bw $^{1/4}$*	*bw $^{2/3}$*	*bw ^{¾}*	*mg/bw*	*mg/bw$^{1/4}$*	*mg/bw$^{2/3}$*	*mg/bw$^{3/4}$*
1	1	1	1	ppm	0.00258	NA	0.00258	0.019	0.3713	0.0712	0.0512	0.1358	0.0069	0.0362	0.0504
1	1	2	10	ppm	0.00285	NA	0.0285	0.019	0.3713	0.0712	0.0512	1.5000	0.0768	0.4003	0.5569
4	1	1	8	ppm	0.018	NA	0.144	0.0975	0.5588	0.2118	0.1745	1.4769	0.2577	0.6798	0.8253
4	1	2	2.5	ppm	0.018	NA	0.045	0.0975	0.5588	0.2118	0.1745	0.4615	0.0805	0.2124	0.2579
4	1	3	0.2	ppm	0.018	NA	0.0036	0.0975	0.5588	0.2118	0.1745	0.0369	0.0064	0.0170	0.0206
8	1	1	0	mg/ml	5.4	5.4	0.0302	0.036	0.4356	0.1090	0.0826	0.8389	0.0693	0.2770	0.3654
8	1	2	0.01	mg/ml	5.4	5.4	0.054	0.036	0.4356	0.1090	0.0826	1.5000	0.1240	0.4953	0.6534
Background levels of copper in drinking water assumed to be 0.01 mg/L (Araya, 2004).															
16	1	1	0	ppm	0.017	NA	0.005	0.13	0.6005	0.2566	0.2165	0.0418	0.0091	0.0212	0.0251
16	1	2	1.5	ppm	0.017	NA	0.0255	0.13	0.6005	0.2566	0.2165	0.1935	0.0419	0.0980	0.1162
16	1	3	3	ppm	0.017	NA	0.051	0.13	0.6005	0.2566	0.2165	0.3622	0.0784	0.1835	0.2175
16	1	4	6	ppm	0.017	NA	0.102	0.13	0.6005	0.2566	0.2165	0.7715	0.1670	0.3908	0.4633
Background levels of copper in drinking water assumed to be 0.01 mg/L (Araya, 2004).															
17	1	1	6	ppm	0.012	NA	0.072	0.0792	0.5305	0.1844	0.1493	0.9091	0.1357	0.3904	0.4823
17	1	2	3	ppm	0.012	NA	0.036	0.0792	0.5305	0.1844	0.1493	0.4545	0.0679	0.1952	0.2411
17	1	3	1.5	ppm	0.012	NA	0.018	0.0792	0.5305	0.1844	0.1493	0.2273	0.0339	0.0976	0.1206
17	2	1	1.5	ppm	0.016	NA	0.024	0.115	0.5823	0.2365	0.1975	0.2087	0.0412	0.1015	0.1215
17	2	2	3	ppm	0.016	NA	0.048	0.115	0.5823	0.2365	0.1975	0.4174	0.0824	0.2030	0.2431
17	2	3	6	ppm	0.016	NA	0.096	0.115	0.5823	0.2365	0.1975	0.8348	0.1649	0.4060	0.4861
17	3	1	1.5	ppm	0.017	NA	0.0255	0.147	0.6192	0.2785	0.2374	0.1735	0.0412	0.0916	0.1074
17	3	2	3	ppm	0.017	NA	0.051	0.147	0.6192	0.2785	0.2374	0.3469	0.0824	0.1831	0.2148
17	3	3	6	ppm	0.017	NA	0.102	0.147	0.6192	0.2785	0.2374	0.6939	0.1647	0.3662	0.4296
18	1	1	0.66	mg/d	NA	NA	0.66	74	2.9330	17.6260	25.2304	0.0089	0.2250	0.0374	0.0262

19	1	1	0	mg/L	0.017	0.0196	0.00731	0.14	0.6117	0.2696	0.2289	0.0522	0.0120	0.0271	0.0319
19	1	2	20	mg/L	0.017	0.0196	0.39931	0.14	0.6117	0.2696	0.2289	2.8522	0.6528	1.4810	1.7447
Background levels of copper in drinking water assumed to be 0.01 mg/L (Araya, 2004).															
24	1	1	6.12	ppm	0.017	NA	0.10404	0.147	0.6192	0.2785	0.2374	0.7078	0.1680	0.3735	0.4382
24	1	2	1.17	ppm	0.017	NA	0.01989	0.147	0.6192	0.2785	0.2374	0.1353	0.0321	0.0714	0.0838
24	1	3	0.83	ppm	0.017	NA	0.01411	0.147	0.6192	0.2785	0.2374	0.0960	0.0228	0.0507	0.0594
24	1	4	0.47	ppm	0.017	NA	0.00799	0.147	0.6192	0.2785	0.2374	0.0544	0.0129	0.0287	0.0337
27	1	1	11	ppm	0.00369	NA	0.04059	0.0246	0.3960	0.0846	0.0621	1.6500	0.1025	0.4799	0.6535
27	1	2	6	ppm	0.00369	NA	0.02214	0.0246	0.3960	0.0846	0.0621	0.9000	0.0559	0.2618	0.3564
27	1	3	5	ppm	0.00369	NA	0.01845	0.0246	0.3960	0.0846	0.0621	0.7500	0.0466	0.2181	0.2970
27	1	4	4	ppm	0.00369	NA	0.01476	0.0246	0.3960	0.0846	0.0621	0.6000	0.0373	0.1745	0.2376
27	1	5	3	ppm	0.00369	NA	0.01107	0.0246	0.3960	0.0846	0.0621	0.4500	0.0280	0.1309	0.1782
27	1	6	2	ppm	0.00369	NA	0.00738	0.0246	0.3960	0.0846	0.0621	0.3000	0.0186	0.0873	0.1188
27	1	7	1	ppm	0.00369	NA	0.00369	0.0246	0.3960	0.0846	0.0621	0.1500	0.0093	0.0436	0.0594
31	1	1	0.785	mg/d	NA	NA	0.785	70	2.8925	16.9850	24.2005	0.0112	0.2714	0.0462	0.0324
31	1	2	1.68	mg/d	NA	NA	1.68	70	2.8925	16.9850	24.2005	0.0240	0.5808	0.0989	0.0694
32	1	1	5.79	mg/kg f	0.02	NA	0.1158	0.3727	0.7813	0.5179	0.4770	0.3107	0.1482	0.2236	0.2428
32	1	2	0.46	mg/kg f	0.02	NA	0.0092	0.3727	0.7813	0.5179	0.4770	0.0247	0.0118	0.0178	0.0193
33	1	1	0.57	mcg/g f	0.021	NA	0.01197	0.216	0.6817	0.3600	0.3168	0.0554	0.0176	0.0333	0.0378
33	1	2	5	mcg/g f	0.021	NA	0.105	0.216	0.6817	0.3600	0.3168	0.4861	0.1540	0.2917	0.3314
34	1	1	0.2	mcg/g f	0.018	NA	0.0036	0.1668	0.6391	0.3030	0.2610	0.0216	0.0056	0.0119	0.0138
34	1	2	10	mcg/g f	0.018	NA	0.18	0.1668	0.6391	0.3030	0.2610	1.0791	0.2817	0.5940	0.6896
37	1	1	1.6	mg/d	NA	NA	1.6	79	2.9813	18.4113	26.4984	0.0203	0.5367	0.0869	0.0604
37	1	2	0.7	mg/d	NA	NA	0.7	79	2.9813	18.4113	26.4984	0.0089	0.2348	0.0380	0.0264
38	1	1	0.6	µg/g f	0.017	NA	0.0102	0.161	0.6334	0.2959	0.2542	0.0634	0.0161	0.0345	0.0401

38	1	2	6	µg/g f	0.017	NA	0.102	0.161	0.6334	0.2959	0.2542	0.6335	0.1610	0.3447	0.4013
38	2	1	0.6	µg/g f	0.0135	NA	0.0081	0.0961	0.5568	0.2098	0.1726	0.0843	0.0145	0.0386	0.0469
38	2	2	6	µg/g f	0.0135	NA	0.081	0.0961	0.5568	0.2098	0.1726	0.8429	0.1455	0.3861	0.4693
39	1	1	0.8	mg/kg/d	554	NA	0.4432	20	2.1147	7.3681	9.4574	0.0222	0.2096	0.0602	0.0469
39	1	2	6.4	mg/kg/d	554	NA	3.5456	20	2.1147	7.3681	9.4574	0.1773	1.6766	0.4812	0.3749
40	1	1	0.4	g/kg f	0.016	NA	0.0064	0.1326	0.6034	0.2600	0.2197	0.0483	0.0106	0.0246	0.0291
40	1	2	5.2	g/kg f	0.016	NA	0.0832	0.1326	0.6034	0.2600	0.2197	0.6275	0.1379	0.3200	0.3786
41	1	1	0.15	mg/kg f	0.021	NA	0.00315	0.223	0.6872	0.3677	0.3245	0.0141	0.0046	0.0086	0.0097
41	1	2	10	mg/kg f	0.021	NA	0.21	0.223	0.6872	0.3677	0.3245	0.9417	0.3056	0.5711	0.6471
44	1	1	1	mg/kg f	0.019	NA	0.019	0.179	0.6504	0.3176	0.2752	0.1061	0.0292	0.0598	0.0690
44	1	2	6	mg/kg f	0.019	NA	0.114	0.179	0.6504	0.3176	0.2752	0.6369	0.1753	0.3589	0.4143
45	1	1	6.2	µmol/kg f	0.017	NA	0.0067	0.161	0.6334	0.2959	0.2542	0.0416	0.0106	0.0226	0.0264
45	1	2	92.4	µmol/kg f	0.017	NA	0.1	0.161	0.6334	0.2959	0.2542	0.6211	0.1579	0.3379	0.3934
47	1	1	0.6	µg/g f	0.015	NA	0.009	0.1265	0.5964	0.2520	0.2121	0.0711	0.0151	0.0357	0.0424
47	1	2	6	µg/g f	0.015	NA	0.09	0.1265	0.5964	0.2520	0.2121	0.7115	0.1509	0.3571	0.4243
50	1	1	0.44	ppm	0.00407	NA	0.0018	0.0271	0.4057	0.0902	0.0668	0.0661	0.0044	0.0198	0.0268
50	1	2	4.98	ppm	0.00407	NA	0.0203	0.0271	0.4057	0.0902	0.0668	0.7479	0.0500	0.2247	0.3035
51	1	1	0.6	mg/kg f	0.018	NA	0.0108	0.304	0.7425	0.4521	0.4094	0.0355	0.0145	0.0239	0.0264
51	1	2	6	mg/kg f	0.018	NA	0.108	0.304	0.7425	0.4521	0.4094	0.3553	0.1454	0.2389	0.2638
52	1	1	0.4	mg/kg f	10.1	NA	0.004	0.271	0.7215	0.4188	0.3756	0.0148	0.0055	0.0096	0.0106
52	1	2	5.7	mg/kg f	10.1	NA	0.053	0.271	0.7215	0.4188	0.3756	0.1956	0.0735	0.1266	0.1411
52	2	1	0.4	mg/kg f	13.7	NA	0.0055	0.325	0.7550	0.4727	0.4304	0.0169	0.0073	0.0116	0.0128
52	2	2	5.7	mg/kg f	13.7	NA	0.089	0.325	0.7550	0.4727	0.4304	0.2738	0.1179	0.1883	0.2068

53	1	1	0	mg/L	NA	NA	0.007	0.108	0.6412	0.3057	0.2636	0.0415	0.0109	0.0230	0.0266
53	1	2	40	mg/L	NA	0.0151	0.604	0.108	0.6412	0.3057	0.2636	1.4414	0.3799	0.7969	0.9242
Background levels of copper in drinking water assumed to be 0.01 mg/L (Araya, 2004).															
55	1	1	0.6	ppm	0.02	NA	0.012	0.358	0.7735	0.5042	0.4628	0.0335	0.0155	0.0238	0.0259
55	1	2	25	ppm	0.02	NA	0.5	0.358	0.7735	0.5042	0.4628	1.3966	0.6464	0.9917	1.0803
58	1	1	0.6	mg/kg f	0.0034	NA	0.00204	0.02276	0.3884	0.0803	0.0586	0.0896	0.0053	0.0254	0.0348
58	1	2	2	mg/kg f	0.0034	NA	0.0068	0.02276	0.3884	0.0803	0.0586	0.2988	0.0175	0.0847	0.1160
58	1	3	6	mg/kg f	0.0034	NA	0.0204	0.02276	0.3884	0.0803	0.0586	0.8963	0.0525	0.2540	0.3481
62	1	1	2.8	mg/kg f	0.018	NA	0.0504	0.315	0.7492	0.4630	0.4205	0.1600	0.0673	0.1089	0.1199
62	1	2	6.6	mg/kg f	0.018	NA	0.1188	0.315	0.7492	0.4630	0.4205	0.3771	0.1586	0.2566	0.2825
66	1	1	0.2	µg/g f	0.018	NA	0.0036	0.161	0.6334	0.2959	0.2542	0.0224	0.0057	0.0122	0.0142
66	1	2	1	µg/g f	0.018	NA	0.018	0.161	0.6334	0.2959	0.2542	0.1118	0.0284	0.0608	0.0708
66	1	3	2	µg/g f	0.018	NA	0.036	0.161	0.6334	0.2959	0.2542	0.2236	0.0568	0.1216	0.1416
66	1	4	3	µg/g f	0.018	NA	0.054	0.161	0.6334	0.2959	0.2542	0.3354	0.0852	0.1825	0.2125
66	1	5	4	µg/g f	0.018	NA	0.072	0.161	0.6334	0.2959	0.2542	0.4472	0.1137	0.2433	0.2833
67	1	1	0.35	mg/kg f	0.003	NA	0.00105	0.02	0.3761	0.0737	0.0532	0.0525	0.0028	0.0143	0.0197
67	1	2	6	mg/kg f	0.003	NA	0.018	0.02	0.3761	0.0737	0.0532	0.9000	0.0479	0.2443	0.3385
68	1	1	1.05	mg/kg f	0.002	NA	0.0021	0.01675	0.3598	0.0655	0.0466	0.1254	0.0058	0.0321	0.0451
68	1	2	6.4	mg/kg f	0.002	NA	0.0128	0.01675	0.3598	0.0655	0.0466	0.7642	0.0356	0.1955	0.2749
70	1	1	0.79	mg/kg	0.017	0.02254	0.01343	0.161	0.6334	0.2959	0.2542	0.0834	0.0212	0.0454	0.0528
70	1	2	3.79	mg/kg	0.017	0.02254	0.1094	0.161	0.6334	0.2959	0.2542	0.6795	0.6795	0.3697	0.4304
71	1	1	0.78	mg/d	NA	NA	0.78	70	2.8925	16.9850	24.2005	0.0111	0.2697	0.0459	0.0322
72	1	1	0.79	µg/ml	0.016	18.62	0.01264	0.133	0.6039	0.2606	0.2202	0.0950	0.0209	0.0485	0.0574
72	1	2	3.79	µg/ml	0.016	18.62	0.0706	0.133	0.6039	0.2606	0.2202	0.5308	0.1169	0.2710	0.3206

73	1	1	0.79	µg/ml	0.016	18.62	0.01264	0.133	0.6039	0.2606	0.2202	0.0950	0.0209	0.0485	0.0574
73	1	2	3.79	µg/ml	0.016	18.62	0.0706	0.133	0.6039	0.2606	0.2202	0.5308	0.1169	0.2710	0.3206
74	1	1	0.79	µg/ml	0.016	18.62	0.01264	0.133	0.6039	0.2606	0.2202	0.0950	0.0209	0.0485	0.0574
74	1	2	3.79	µg/ml	0.016	18.62	0.0706	0.133	0.6039	0.2606	0.2202	0.5308	0.1169	0.2710	0.3206
76	1	1	0.3	mg/kg f	0.0032	NA	0.00096	0.0221	0.3856	0.0788	0.0573	0.0434	0.0025	0.0122	0.0167
76	1	2	8.4	mg/kg f	0.0032	NA	0.02688	0.0221	0.3856	0.0788	0.0573	1.2163	0.0697	0.3413	0.4690
77	1	1	1	mg/kg f	0.019	NA	0.019	0.249	0.7064	0.3958	0.3525	0.0763	0.0269	0.0480	0.0539
77	1	2	7	mg/kg f	0.019	NA	0.133	0.249	0.7064	0.3958	0.3525	0.5341	0.1883	0.3360	0.3773
78	1	1	2.7	mg/kg f	0.02	NA	0.054	0.258	0.7127	0.4053	0.3620	0.2093	0.0758	0.1332	0.1492
78	1	2	6.2	mg/kg f	0.02	NA	0.124	0.258	0.7127	0.4053	0.3620	0.4806	0.1740	0.3060	0.3425
81	1	1	0.8	mg/kg f	0.014	NA	0.0112	0.0985	0.5602	0.2133	0.1758	0.1137	0.0200	0.0525	0.0637
81	1	2	1.7	mg/kg f	0.014	NA	0.0238	0.0985	0.5602	0.2133	0.1758	0.2416	0.0425	0.1116	0.1354
81	1	3	6.7	mg/kg f	0.014	NA	0.0938	0.0985	0.5602	0.2133	0.1758	0.9523	0.1674	0.4398	0.5335
83	1	1	7.9	µmol/kg f	0.015	NA	0.00753	0.116	0.5836	0.2379	0.0256	0.0649	0.0129	0.0317	0.2946
83	1	2	125.9	µmol/kg f	0.015	NA	0.12	0.116	0.5836	0.2379	0.2039	1.0345	0.2056	0.5045	0.5886
84	1	1	20	mg/L	0.018	19.18	0.39152	0.137	0.6084	0.2658	0.2252	2.8578	0.6435	1.4732	1.7387
84	1	2	0	mg/L	0.018	NA	0.00792	0.137	0.6084	0.2658	0.2252	0.0578	0.0130	0.0298	0.0352
Background levels of copper in drinking water assumed to be 0.01 mg/L (Araya, 2004).															
85	1	1	0	ppm	0.02	32.62	0.008	0.233	0.6948	0.3786	0.3354	0.0343	0.0115	0.0211	0.0239
85	1	2	20	ppm	0.02	32.62	0.6604	0.233	0.6948	0.3786	0.3354	2.8343	0.9505	1.7441	1.9692
Purified base diet contains 0.4 mg/kg															
86	1	1	0.4	mg/kg/d	0.009	NA	0.0036	0.05753	0.4897	0.1490	0.1175	0.0626	0.0074	0.0242	0.0306
86	1	2	4	mg/kg/d	0.009	NA	0.036	0.05753	0.4897	0.1490	0.1175	0.6258	0.0735	0.2416	0.3065
89	1	1	0.6	mg/kg f	0.019	NA	0.0114	0.181	0.6523	0.3200	0.2775	0.0630	0.0175	0.0356	0.0411

89	1	2	7.5	mg/kg f	0.019	NA	0.1425	0.181	0.6523	0.3200	0.2775	0.7873	0.2185	0.4453	0.5135
90	1	1	0	mg/kg f	0.02	NA	0.005	0.268	0.7195	0.4157	0.3725	0.0201	0.0075	0.0130	0.0145
90	1	2	1.5	mg/kg f	0.02	NA	0.03	0.268	0.7195	0.4157	0.3725	0.1119	0.0417	0.0722	0.0805
90	1	3	3	mg/kg f	0.02	NA	0.06	0.268	0.7195	0.4157	0.3725	0.2239	0.0834	0.1443	0.1611
90	1	4	4.5	mg/kg f	0.02	NA	0.09	0.268	0.7195	0.4157	0.3725	0.3358	0.1251	0.2165	0.2416
90	1	5	6	mg/kg f	0.02	NA	0.12	0.268	0.7195	0.4157	0.3725	0.4478	0.1668	0.2887	0.3222
Background levels of copper in drinking water assumed to be 0.01 mg/L (Araya, 2004).															
91	1	1	0.37	mg/kg	0.019	NA	0.00703	0.1807	0.6520	0.3196	0.2772	0.0389	0.0108	0.0220	0.0254
91	1	2	0.79	mg/kg	0.019	NA	0.01501	0.1807	0.6520	0.3196	0.2772	0.0831	0.0230	0.0470	0.0542
91	1	3	2.45	mg/kg	0.019	NA	0.04655	0.1807	0.6520	0.3196	0.2772	0.2576	0.0714	0.1456	0.1680
91	1	4	7.28	mg/kg	0.019	NA	0.13832	0.1807	0.6520	0.3196	0.2772	0.7655	0.2122	0.4328	0.4991
92	1	1	0.1	mg/kg f	0.018	NA	0.0018	0.199	0.6679	0.3409	0.2979	0.0090	0.0027	0.0053	0.0060
92	1	2	10	mg/kg f	0.018	NA	0.18	0.199	0.6679	0.3409	0.2979	0.9045	0.2695	0.5281	0.6041
95	1	1	9.4	µmol/kg f	0.015	NA	0.009	0.122	0.5910	0.2460	0.2064	0.0738	0.0152	0.0366	0.0436
95	1	2	103.9	µmol/kg f	0.015	NA	0.1	0.122	0.5910	0.2460	0.2064	0.8197	0.1692	0.4065	0.4844
96	1	1	1.3	mg/kg f	0.02	NA	0.026	0.377	0.7836	0.5219	0.4811	0.0690	0.0332	0.0498	0.0540
96	1	2	2.8	mg/kg f	0.02	NA	0.056	0.377	0.7836	0.5219	0.4811	0.1485	0.0715	0.1073	0.1164
96	1	3	6.7	mg/kg f	0.02	NA	0.134	0.377	0.7836	0.5219	0.4811	0.3554	0.1710	0.2568	0.2785
100	1	1	0.6	mg/kg f	0.019	NA	0.0114	0.181	0.6523	0.3200	0.2775	0.0630	0.0175	0.0356	0.0411
100	1	2	7.5	mg/kg f	0.019	NA	0.1425	0.181	0.6523	0.3200	0.2775	0.7873	0.2185	0.4453	0.5135
102	1	1	0.57	mg/1000kcal	NA	NA	1.6245	70	2.8925	16.9850	24.2005	0.0124	0.3008	0.0512	0.0359
102	1	2	1.61	mg/100kcal	NA	NA	4.5885	70	2.8925	16.9850	24.2005	0.0197	0.4771	0.0812	0.0570
106	1	1	0.57	mg/kg f	0.02	NA	0.0114	0.381	0.7857	0.5256	0.4849	0.0299	0.0145	0.0217	0.0235
106	1	2	5	mg/kg f	0.02	NA	0.1	0.381	0.7857	0.5256	0.4849	0.2625	0.1273	0.1903	0.2062

107	1	1	0.06	mg/kg	0.019	NA	0.00114	0.175	0.6468	0.3129	0.2706	0.0065	0.0018	0.0036	0.0042
107	1	2	20.03	mg/kg	0.019	NA	0.38114	0.175	0.6468	0.3129	0.2706	2.1779	0.5893	1.2182	1.4087
108	1	1	5	mg/kg	0.02	NA	0.1	0.25	0.7071	0.3969	0.3536	0.4	0.1414	0.2520	0.2828
108	1	2	2.5	mg/kg	0.02	NA	0.05	0.25	0.7071	0.3969	0.3536	0.2	0.0707	0.1260	0.1414
108	1	3	0.75	mg/kg	0.02	NA	0.015	0.25	0.7071	0.3969	0.3536	0.06	0.0212	0.0378	0.0424
115	1	1	6	ppm	0.0041	NA	0.0243	0.027	0.4054	0.09	0.0666	0.9	0.0599	0.27	0.3648
115	1	2	0.5	ppm	0.0041	NA	0.0020	0.027	0.4054	0.09	0.0666	0.075	0.0050	0.0225	0.0304
118	1	1	6.19	mg/kg	0.017	NA	0.10523	0.12	0.5886	0.2433	0.2039	0.8769	0.1788	0.4325	0.5161
118	1	2	0.43	mg/kg	0.017	NA	0.00731	0.12	0.5886	0.2433	0.2039	0.0609	0.0124	0.0300	0.0359
119	1	1	6	mg/kg	0.0178	NA	0.1068	0.12	0.5886	0.2433	0.2039	0.8900	0.1815	0.4390	0.5238
119	1	2	0.5	mg/kg	0.0178	NA	0.0089	0.12	0.5886	0.2433	0.2039	0.0742	0.0151	0.0366	0.0437
120	1	1	5.6	mg/kg	0.017	NA	0.0952	0.125	0.5946	0.25	0.2102	0.7616	0.7616	0.3808	0.4529
120	1	2	0.66	mg/kg	0.017	NA	0.01122	0.125	0.5946	0.25	0.2102	0.08976	0.08976	0.04488	0.0534
121	1	1	5.3	µg/g	0.013	NA	0.0689	0.085	0.5400	0.1933	0.1574	0.8106	0.1276	0.3564	0.4377
121	1	2	0.8	µg/g	0.013	NA	0.0104	0.085	0.5400	0.1933	0.1574	0.1224	0.0193	0.0538	0.0661
122	1	1	2.59	mg/d	NA	NA	2.59	87	3.0541	19.6342	28.4865	0.0298	0.8480	0.1319	0.0909
122	1	2	0.59	mg/d	NA	NA	0.59	87	3.0541	19.6342	28.4865	0.0068	0.1932	0.0300	0.0207
123	1	1	6	mg/kg	0.017	NA	0.102	0.13	0.6005	0.2566	0.2165	0.7846	0.1699	0.3975	0.4711
123	1	2	0.5	mg/kg	0.017	NA	0.0085	0.13	0.6005	0.2566	0.2165	0.0654	0.0142	0.0331	0.0393
125	1	1	5.88	mg/kg	0.02	NA	0.1176	0.44	0.8144	0.5785	0.5402	0.2673	0.1444	0.2033	0.2177
125	1	2	2.94	mg/kg	0.02	NA	0.0588	0.44	0.8144	0.5785	0.5402	0.1336	0.0722	0.1016	0.1088
125	1	3	1.62	mg/kg	0.02	NA	0.0324	0.44	0.8144	0.5785	0.5402	0.0736	0.0398	0.0560	0.0600

129	1	1	6	mg/d	NA	NA	6	78.4	2.9756	18.3180	26.3474	0.0765	2.0164	0.3275	0.2277
129	1	2	1.6	mg/d	NA	NA	1.6	78.4	2.9756	18.3180	26.3474	0.0204	0.5377	0.0873	0.0607
129	1	3	0.7	mg/d	NA	NA	0.7	78.4	2.9756	18.3180	26.3474	0.0089	0.2352	0.0382	0.0266
133	1	1	6	mg/kg	0.018	NA	0.108	0.167	0.6393	0.3033	0.2612	0.6467	0.1689	0.3561	0.4134
133	1	2	3	mg/kg	0.018	NA	0.054	0.167	0.6393	0.3033	0.2612	0.3234	0.0845	0.1781	0.2067
133	1	3	2.5	mg/kg	0.018	NA	0.045	0.167	0.6393	0.3033	0.2612	0.2695	0.0704	0.1484	0.1723
133	1	4	2	mg/kg	0.018	NA	0.036	0.167	0.6393	0.3033	0.2612	0.2156	0.0563	0.1187	0.1378
133	1	5	1.5	mg/kg	0.018	NA	0.027	0.167	0.6393	0.3033	0.2612	0.1617	0.0422	0.0890	0.1034
133	1	6	1	mg/kg	0.018	NA	0.018	0.167	0.6393	0.3033	0.2612	0.1078	0.0282	0.0594	0.0689
133	1	7	0.63	mg/kg	0.018	NA	0.01134	0.167	0.6393	0.3033	0.2612	0.0679	0.0177	0.0374	0.0434
133	2	1	6	mg/kg	0.015	NA	0.09	0.155	0.6275	0.2886	0.2470	0.5806	0.1434	0.3119	0.3643
133	2	2	3	mg/kg	0.015	NA	0.045	0.155	0.6275	0.2886	0.2470	0.2903	0.0717	0.1560	0.1822
133	2	3	2.5	mg/kg	0.015	NA	0.0375	0.155	0.6275	0.2886	0.2470	0.2419	0.0598	0.1300	0.1518
133	2	4	2	mg/kg	0.015	NA	0.03	0.155	0.6275	0.2886	0.2470	0.1935	0.0478	0.1040	0.1214
133	2	5	1.5	mg/kg	0.015	NA	0.0225	0.155	0.6275	0.2886	0.2470	0.1452	0.0359	0.0780	0.0911
133	2	6	1	mg/kg	0.015	NA	0.015	0.155	0.6275	0.2886	0.2470	0.0968	0.0239	0.0520	0.0607
133	2	7	0.63	mg/kg	0.015	NA	0.00945	0.155	0.6275	0.2886	0.2470	0.0610	0.0151	0.0327	0.0383
137	1	1	5.7	mg/kg	0.022	NA	0.1254	0.5	0.8409	0.6300	0.5946	0.2508	0.1491	0.1991	0.2109
137	1	2	3.1	mg/kg	0.022	NA	0.0682	0.5	0.8409	0.6300	0.5946	0.1364	0.0811	0.1083	0.1147
137	1	3	1.65	mg/kg	0.022	NA	0.0356	0.5	0.8409	0.6300	0.5946	0.0712	0.0423	0.0565	0.0599
141	1	1	20	mg/L	0.02	37.5	0.708	0.25	0.7071	0.3969	0.3536	2.832	1.0013	1.7840	2.0025
141	1	2	0	mg/L	0.02	37.5	0.008	0.25	0.7071	0.3969	0.3536	0.032	0.0113	0.0202	0.0226
141	2	1	20	mg/L	3	3	0.0612	0.02	0.3761	0.0737	0.0532	3.06	0.1627	0.8306	1.1507
141	2	2	0	mg/L	3	3	0.0012	0.02	0.3761	0.0737	0.0532	0.06	0.0032	0.0163	0.0226
Background levels of copper in drinking water assumed to be 0.01 mg/L (Araya, 2004).															
142	1	1	7.28	mg/kg	0.016	NA	0.1165	0.125	0.5946	0.25	0.2102	0.932	0.1959	0.466	0.5542
142	1	2	2.45	mg/kg	0.016	NA	0.0392	0.125	0.5946	0.25	0.2102	0.3136	0.0659	0.1568	0.1865
142	1	3	0.79	mg/kg	0.016	NA	0.0126	0.125	0.5946	0.25	0.2102	0.1008	0.0212	0.0504	0.0599

142	1	4	0.37	mg/kg	0.016	NA	0.0059	0.125	0.5946	0.25	0.2102	0.0472	0.0099	0.0236	0.0281
143	1	1	6	mg/kg	0.016	NA	0.096	0.125	0.5946	0.25	0.2102	0.768	0.1615	0.384	0.4567
143	1	2	0.3	mg/kg	0.016	NA	0.0048	0.125	0.5946	0.25	0.2102	0.0384	0.0081	0.0192	0.0228
144	1	1	6.18	mg/kg	0.017	NA	0.1051	0.125	0.5946	0.25	0.2102	0.8408	0.1768	0.4204	0.4999
144	1	2	0.29	mg/kg	0.017	NA	0.0049	0.125	0.5946	0.25	0.2102	0.0392	0.0082	0.0196	0.0233
148	1	1	10.5	mg/kg	0.021	NA	0.2205	0.232	0.6940	0.3776	0.3343	0.9504	0.3177	0.584	0.6596
148	1	2	0.43	mg/kg	0.021	NA	0.009	0.232	0.6940	0.3776	0.3343	0.0388	0.0130	0.024	0.0269
149	1	1	6.26	mg/kg	0.017	NA	0.1064	0.155	0.6275	0.2886	0.2470	0.6865	0.1696	0.369	0.4307
149	1	2	0.16	mg/kg	0.017	NA	0.0027	0.155	0.6275	0.2886	0.2470	0.0174	0.0043	0.009	0.0109
167	1	1	7.19	mg/kg	0.015	NA	0.1079	0.1	0.5623	0.2154	0.1778	1.0790	0.1919	0.501	0.6068
167	1	2	0.78	mg/kg	0.015	NA	0.0117	0.1	0.5623	0.2154	0.1778	0.1170	0.0208	0.054	0.0658
177	1	1	5.6	mg/kg	0.017	NA	0.0952	0.125	0.5946	0.2500	0.2102	0.7616	0.1601	0.381	0.4529
177	1	2	0.33	mg/kg	0.017	NA	0.00528	0.125	0.5946	0.2500	0.2102	0.0422	0.0089	0.021	0.0251
179	1	1	6.18	mg/kg	0.016	NA	0.0989	0.125	0.5946	0.2500	0.2102	0.7912	0.1663	0.396	0.4705
179	1	2	0.29	mg/kg	0.016	NA	0.0046	0.125	0.5946	0.2500	0.2102	0.0368	0.0077	0.018	0.0219
183	1	1	5.4	mg/kg	0.016	NA	0.0864	0.125	0.5946	0.2500	0.2102	0.6912	0.1453	0.346	0.4110
183	1	2	0.3	mg/kg	0.016	NA	0.0048	0.125	0.5946	0.2500	0.2102	0.0384	0.0081	0.019	0.0228
185	1	1	6	mg/kg	0.017	NA	0.1071	0.152	0.6244	0.2848	0.2434	0.7046	0.1715	0.376	0.4400
185	1	2	0	mg/kg	0.017	NA	0.0051	0.152	0.6244	0.2848	0.2434	0.0336	0.0082	0.018	0.0210
Background levels of copper in drinking water assumed to be 0.01 mg/L (Araya, 2004).															
202	1	1	5	mg/kg	0.017	NA	0.085	0.125	0.5946	0.2500	0.2102	0.6800	0.1430	0.340	0.4043
202	1	2	0.25	mg/kg	0.017	NA	0.004	0.125	0.5946	0.2500	0.2102	0.0320	0.0067	0.016	0.0190

202	2	1	5	mg/kg	0.016	NA	0.075	0.115	0.5823	0.2365	0.1975	0.6522	0.1288	0.317	0.3798
202	2	2	0.25	mg/kg	0.016	NA	0.00375	0.115	0.5823	0.2365	0.1975	0.0326	0.0064	0.016	0.0190
211	1	1	5.7	mg/kg	0.021	NA	0.1197	0.5	0.8409	0.6300	0.5946	0.2394	0.1423	0.1900	0.2013
211	1	2	1.1	mg/kg	0.021	NA	0.0231	0.5	0.8409	0.6300	0.5946	0.0462	0.0275	0.0367	0.0388

Note. Ref ID #, reference ID number (corresponds with references and ID number in Tables 8 and 9); Exp, experiment number within the publication; Grp, group number within experiment; Base, reported dose of copper; BW, body weight; Cu, copper; ppm, parts per million; mg/ml, milligrams of copper per milliliter of water; mg/d, milligrams of copper per day; mg/L, milligrams of copper per liter of water; mg/kg f, milligrams of copper per kilogram of feed; µg /g f, micrograms of copper per gram of feed; g/kg f, grams of copper per kilogram of feed; µmol/kg f, micromoles of copper per kilogram of feed; µg/ml, micrograms of copper per millimeter of water; mg/1000kcal, milligrams of copper per 1000 kilocalories.

APPENDIX F: COPPER DATABASE – DEFINED BY RESPONSES TO ELEVATED AND DEFICIENT COPPER INTAKE

Table F1: Responses Associated with Studies on Copper Excess

Reference	*Species*	*Copper species/ study type/ exposure route/duration/sex*	*Effects*	*Dose groups*	*Severity scores*	*Group Size*
Alissa et al., 2004	Rabbits	NS/ Subchronic / Dietary / 84 days / Males	Increased body weight, increased plasma copper, increase liver copper, increased liver zinc, increased zinc in aorta, increased liver enzyme activity,	3.7 mg/d 350 mg/d	0 3	8 8
Araya et al. 2003	Humans	$CuSO_4$ / Acute / Drinking water / 1 time dose / Both Males & Females	Increased antral area and nausea	0 mg/l 10 mg/l	0 4	30
Araya et al. 2003b	Humans	$CuSO_4$/ Acute / Drinking water / 1 dose / Females	Increased nausea	0 mg/l 2 mg/l 4 mg/l 6 mg/l 8 mg/l	0 0 0 4 4	269
Araya et al. 2003c	Humans	$CuSO_4$ / Subchronic / Drinking water / 60 days / Both Males & Females	GI symptoms	0.01 mg/l 2 mg/l 4 mg/l 6 mg/l	0 0 0 4	60
Araya et al. 2004	Humans	$CuSO_4$ / Subchronic / Drinking water / 60 days / Both Males & Females	GI symptoms	0.02 mg/l 2 mg/l 4 mg/l 6 mg/l	0 0 0 4	343 327 355 340
Armstrong et al. 2004	Pigs	$CuSO_4$ & CuCit / Dietary / 40 days / Both Males & Females	Improved growth rate and feed efficiency	10 ppm 135 ppm 260 ppm	0 3 3	66 66 66

				15 ppm 46 ppm 77 ppm 140 ppm	0 0 0 3	66 66 66 66
Baker et al., 1999	Humans	$CuSO_4$ / Subacute / Capsule / 42 days	No effect of copper supplementation on biochemical markers of bone metabolism	0 mg/day 3 mg/day 6 mg/day	0 0 0	12 12 12
Baker et al., 1999	Humans	$CuSO_4$ / Subacute / Capsule / 42 days	No effect of copper supplementation on biochemical markers of bone metabolism	1.6 mg/day 6.0 mg/day	0 0	11 11
Becaria et al., 2006	Mice	$CuSO_4$ / Subchronic / Drinking water / 84 days / Males	Increased serum TNF alpha levels, increased MDA levels in brain	0 ppm 2 ppm	0 3	6 6
Cristofori et al., 1992	Rats	NS / Chronic / Dietary / 210 days / Males & Females	Increased liver, kidney and skeletal Cu and increased liver ALT.	5 ppm 200 ppm	0 2	10 10
		NS / Chronic / Dietary / 350 days / Males & Females	Increased liver, kidney and skeletal Cu and increased serum ALP.	5 ppm 200 ppm	0 2	10 10
Cromwell et al., 1989	Pigs	$CuSO_4$ / Subacute / Dietary / 28 days	Increased weight gain, decrease in feed intake/body weight gain ratio and increased liver copper burden.	0 ppm 125 ppm 250 ppm	0 3 3	8 8 8
		CuO / Subacute / Dietary / 28 days	No effects.	0 ppm 125 ppm 250 ppm	0 0 0	8 8 8
Cunnane et al., 1985	Rats	NS / Subchronic / Dietary / 84 days	Increase in body weight;	6 mg/kg/day	0	10

			decrease in liver and heart weight; and altered levels of blood lipids.	250 mg/kg/day	3	10
Davis 2002b	Pigs	NS / Subacute / Dietary / 10 days / Males & Females	Increased body weight	20 ppm 195 ppm	0 3	54 54
Fuentealba et al., 1989	Rats	NS / Subacute / Dietary / 7 days	Liver necrosis and increased liver Cu burden.	20 ppm 1500 ppm	0 4	4 4
		NS / Subacute / Dietary / 28 days	Liver necrosis and increased liver Cu burden.	20 ppm 1500 ppm	0 4	4 4
		NS / Subchronic / Dietary / 56 days	Liver necrosis and increased liver Cu burden.	20 ppm 1500 ppm	0 4	4 4
		NS / Subchronic / Dietary / 84 days	Liver necrosis and increased liver Cu burden.	20 ppm 1500 ppm	0 4	4 4
		NS/ Chronic / Dietary / 112 days	Liver necrosis and increased liver Cu burden.	20 ppm 1500 ppm	0 4	4 4
Fuentealba et al., 2000	Rats	$CuSO_4$/Chronic/Dietary/126 days	Increased liver Cu, decreased hepatic metallothein, altered levels of Alanine Amine Transferase and sorbitol dehydrogenase	0 ppm 1500 ppm	0 3	5 5
Giovanetti et al., 1998	Mice	$CuSO_4$ / Subacute / Dietary / 28 days	Altered levels of GSSG, gluthione content, Cu-Zn SOD, and Cu burden in the lungs. Altered lung weight. Altered liver copper burden and weight.	4.98 ppm 200 ppm	0 3	6 6
Goldschmith et al., 2005	Rats – A	$CuSO_4$ / Subacute / Drinking Water / 20 days / Males & Females	Increased brain copper, reduced synaptic sensibility and facilitation capacity (brain	0.12 mg/d 12.12 mg/d	0 4	23 23

			function)			
Gurel et al., 2007	Rats	NS / Subchronic / Drinking water / 60 days / Females	Increased liver, kidney and lung copper, increased MT levels in brain and kidney and increased apoptotic index in liver	0 mg/l 100 mg/l 400 mg/l	0 4 4	8 8 8
Gross et al., 1989	Rats	$Cu(CH_3COO)_2$ / Chronic / Drinking Water/ 252 days	Altered liver copper burden, levels of liver function parameters and liver function.	0% 0.0125%	0 3	9 9
Haywood et al., 1980	Rats	NS/Subacute/Dietary/7days	Increased liver and kidney Cu	0 ppm 2000 ppm	0 1	4 4
		NS/Subacute/Dietary/14days	Increased liver and kidney Cu, liver histopathology.	0 ppm 2000 ppm	0 4	4 4
		NS/Subacute/Dietary/21days	Increase liver and kidney Cu, liver and kidney histopathology	0 ppm 2000 ppm	0 4	4 4
		NS/Subchronic/Dietary/42days	Increase liver and kidney Cu, liver and kidney histopathology	0 ppm 2000 ppm	0 4	4 4
		NS/Subchronic/Dietary/63days	Increase liver and kidney Cu, liver and kidney histopathology	0 ppm 2000 ppm	0 4	4 4
		NS/Subchronic/Dietary/105days	Increase liver and kidney Cu, liver and kidney histopathology	0 ppm 2000 ppm	0 4	4 4
Haywood et al., 1985	Rats	NA / Subacute,/ Dietary / 7days	Necrobiotic changes in liver in highest dose group, increased liver copper burden.	10 mg/kg 3000 mg/kg 4000 mg/kg 5000 mg/kg	0 1 1 1	4 4 4 4

		6000 mg/kg	4	4
NA/Subacute/Dietary/14 days	Liver and kidney histopathology. Increased copper burden in liver and kidney.	10 mg/kg	0	4
		3000 mg/kg	4	4
		4000 mg/kg	4	4
		5000 mg/kg	4	4
		6000 mg/kg	4	4
NA/ Subacute/Dietary/21 days	Liver and kidney histopathology. Increase copper burden in liver and kidney.	10 mg/kg	0	4
		3000 mg/kg	4	4
		4000 mg/kg	4	4
		5000 mg/kg	4	4
		6000 mg/kg	4	4
NA/Subacute/Dietary/28 days	Liver and kidney histopathology. Increase copper burden in liver and kidney.	10 mg/kg	0	4
		3000 mg/kg	4	4
		4000 mg/kg	4	4
		5000 mg/kg	4	4
		6000 mg/kg	4	4
NA/Subchronic/Dietary/35 days	Kidney and liver histopathology, extensive necrosis in liver at 6000 mg.kg, increased liver and kidney copper.	10 mg/kg	0	4
		3000 mg/kg	4	4
		4000 mg/kg	4	4
		5000 mg/kg	4	4
		6000 mg/kg	5	4
NA/Subchronic/Dietary/42 days	Kidney and liver histopathology, chronic hepatitis at 6000 mg/kg. Increased liver and kidney copper.	10 mg/kg	0	4
		3000 mg/kg	4	4
		4000 mg/kg	4	4
		5000 mg/kg	4	4
		6000 mg/kg	5	4
NA/Chronic/Dietary/105 days	Kidney and liver histopathology, chronic hepatitis at 6000 mg/kg. Increased liver and kidney copper.	10 mg/kg	0	4
		3000 mg/kg	4	4
		4000 mg/kg	4	4
		5000 mg/kg	4	4
		6000 mg/kg	5	4

Hebert, 1993	Rats	$CuSO_4$/Subacute/Drinking Water/15 days/Males	Decreased body weight, decreased longevity at 3000 and 10000ppm.	0 ppm 300 ppm 1000 ppm 3000 ppm 10000 ppm 30000 ppm	0 0 0 3 6 6	5 5 5 5 5 5
	Mice	$CuSO_4$/Subacute/Drinking Water/15 days/Males	Altered all body tissue histopathology and body weight at three highest doses. Decreased longevity at 3000 and 10000 ppm.	0 ppm 300 ppm 1000 ppm 3000 ppm 10000 ppm 30000 ppm	0 0 0 4 6 6	5 5 5 5 5 5
	Rats	$CuSO_4$/Subacute/Drinking Water/15 days/Females	Decreased longevity at 10000 and 30000 ppm. Altered body weight at three highest doses.	0 ppm 300 ppm 1000 ppm 3000 ppm 10000 ppm 30000 ppm	0 0 0 3 6 6	5 5 5 5 5 5
	Mice	$CuSO_4$/Subacute/Drinking Water/15 days/Females	Decreased final body weight, decreased kidney, liver and altered tissue histopathology in three highest dose groups. Decreased longevity at 10000 and 30000 ppm. Altered brain and lung weights at 4 highest dose groups.	0 ppm 300 ppm 1000 ppm 3000 ppm 10000 ppm 30000 ppm	0 0 3 4 6 6	5 5 5 5 5 5
	Rats	$CuSO_4$/Subacute/Dietary/15 days / Males	Increased liver and kidney copper at highest dose group. Lower liver weight, inflammation of liver, depletion of cells in bone marrow at the 2 highest dose groups.	0 ppm 1000 ppm 2000 ppm 4000 ppm 8000 ppm 16000 ppm	0 0 0 0 4 4	5 5 5 5 5 5

	Rats	$CuSO_4$/Subacute/Dietary/15 days / Females	Inflammation of liver and depletion of cells in bone marrow at the two highest dose groups. Significantly lower liver weight at the three highest dose groups.	0 ppm 1000 ppm 2000 ppm 4000 ppm 8000 ppm 16000 ppm	0 0 0 3 4 4	5 5 5 5 5 5
	Mice	$CuSO_4$/Subacute/Dietary/15 days / Males	Increased brain weights at the two highest dose groups. Increased liver weights and forestomach hyperplasia at the three highest dose groups.	0 ppm 1000 ppm 2000 ppm 4000 ppm 8000 ppm 16000 ppm	0 0 0 4 4 4	5 5 5 5 5 5
	Mice	$CuSO_4$/Subacute/Dietary/15 days / Females	Increased brain and liver weights at the highest dose groups. Forestomach hyperplasia at the three highest dose groups.	0 ppm 1000 ppm 2000 ppm 4000 ppm 8000 ppm 16000 ppm	0 0 0 4 4 4	5 5 5 5 5 5
	Rats	$CuSO_4$/Subchronic/Dietary/92 days / Males	Altered hematrocrit, hemoglobin, at the 2 highest doses. Altered mean cell volume and hemoglobin at the 3 highest doses. Altered erythrocytes, reticulocytes at the highest dose group.	0 ppm 500 ppm 1000 ppm 2000 ppm 4000 ppm 8000 ppm	0 1 3 4 4 4	5 5 5 5 5 5
	Rats	$CuSO_4$/Subchronic/Dietary/92 days / Females	Altered hematocrit and hemoglobin at highest dose group. Altered mean cell volume and hemoglobin at the three highest dose groups.	0 ppm 500 ppm 1000 ppm 2000 ppm 4000 ppm 8000 ppm	0 1 3 4 4 4	5 5 5 5 5 5
	Mice	$CuSO_4$/Chronic/Dietary/92 days /	Altered heart and kidney	0 ppm	0	5

		Males	weights at highest dose group. Altered liver weight and forestomach hyperplasia at three highest dose groups.	1000 ppm 2000 ppm 4000 ppm 8000 ppm 16000 ppm	0 0 4 4 4	5 5 5 5 5
	Mice	$CuSO_4$/Chronic/Dietary/92 days / Females	Altered kidney and thymus weights at the highest dose group. Altered liver weight at the two highest dose groups. Forestomach hyperplasia at the three highest dose groups.	0 ppm 1000 ppm 2000 ppm 4000 ppm 8000 ppm 16000 ppm	0 0 0 4 4 4	5 5 5 5 5 5
Jantsch et al., 1985	Humans	$CuSO_4$ / Acute / Dietary / 1 dose	Hepatoxicity	250 g/day	4	1
Jones et al., 1997	Humans	Copper as glycine-chelate / Subacute / Capsule / 28 days	No effect on blood copper enzyme activities and indicators of cardiovascular disease risk	0 mg/day 2 mg/day	0 0	20 20
Kvietkauskaite et al., 2004	Mice	$CuSO_4$ / Subchronic / Drinking water / 133 days / Males	Decreased body weight, decreased liver weight, increased liver copper, decreased protein in liver, increased cytosis SOD activity, increased liver catalase activity , decreased cells of the immune system	0 mg/kg bw/d 22 mg/kg bw/d 42 mg/kg bw/d	0 3 3	10 10 10
Lai et al., 2005	Rats	$CuSO_4$ / Subacute / Drinking water / 7 days / Males	Decreased calcium in femoral diaphyseal	0 µg/mL 50 µg/mL 100 µg/mL 200 µg/mL	0 0 0 3	6 6 6 6
Massie et al., 1984	Mice	$C_{12}H_{22}CuO_{14}$ / Chronic / Drinking Water / 906 and 776 / Males	Altered body weight. Altered serum, liver, kidney, brain and cardiovascular levels of copper. Decreased lifespan.	0 ppm 317 ppm	0 6	8 8

Mullins et al., 1998	Rats	$CuSO_4$ / Subchronic / Dietary / 42 days / Males	Altered levels of metallothionein in liver, duodenum and kidney.	10 mg/kg 1500 mg/kg	0 2	
Murthy et al., 1981	Rats	$CuSO_4$ / Subacute / Dietary / 30 days	Increase dopamine, norepinephrine, 5-hydroxytrptamine and Cu in brain	0 mg/day 5 mg/day	0 3	6 6
O'Connor et al., 2003	Humans	$CuSO_4$ & Cu Glycine Chelates / Subacute / Capsule / 42 days / Males & Females	Increased serum dioxides, increased WBC cytochrome oxidase	1.23 mg/day 4.23 mg/day 1.23 mg/day 4.23 mg/day 1.23 mg/day 7.23 mg/day	0 1 0 1 0 1	15 15 15 15 15 15
O'Donohue et al., 1993	Humans	NS / Chronic / Capsule / 1095 days / Male	Liver cirrhosis	45 mg/day	4	1
Ozcelik et al., 2002	Rats – A	$CuSO_4$ / Subchronic / Drinking Water / 54 days / Males & Females	Decreased erythrocyte deformability, decreased Hb, decreased erythrocyte count, increased serum copper, increased blood viscosity	0 µg / mL 250 µg/mL	0 3	7 7
Pizarro et al., 1999b	Humans	$CuSO_4$ / Subchronic / Drinking Water / 77 day / Females	Increased GI symptoms	0 mg/l 1 mg/l 3 mg/l 5 mg/l	0 0 4 4	60 60 60 60
Pratt et al., 1985	Humans	$C_{12}H_{22}CuO_{14}$ / Subchronic / Capsule / 84 days	Decrease in serum potassium	0 mg/day 10 mg/day	0 2	7 7
Rana et al., 1980	Rats	$CuSO_4$ / Subacute / Dietary / 20 days / Males	Altered liver weight, growth and body weight. Altered hemoglobin, hematocrit and	0 mg/kg/day 100mg/kg/day	0 4	10 10

			RBC count. Histopathological changes in the liver and kidney			
Turnlund et al., 2004	Humans	NS / Subacute / Capsule / 18 days / Males	Increased superoxide dismutase, increased Cp activity, increased Benzylamine oxidase activity, increased urinary copper, increased hair copper	7.8 mg/d	2	11
Zhang et al., 2000	Rats	$CuSO_4$ / Subchronic / Capsule / 40 days / Both Males & Females	Altered copper burden, serum ALT, liver SOD, RBC SOD activity, liver gluthione peroxidise activity, liver MDA and serum MDA	0 mg/kg/day 500 mg/kg/day	0 3	4 4

Table F2: Responses Associated with Studies on Copper Deficiency

Reference	*Species*	*Copper species/ study type/ exposure route/duration*	*Effects*	*Dose groups*	*Severity scores*	*Group Size*
Ajayi et al. 2005	Rats	$CuCO_3$ / Subchronic / Dietary / 42 days / Males	Impaired body weight, depigmentation of hair, reduced packed cell volume, reduced white blood cell count, altered metabolism as reflected by liver and kidney content of trace elements	0.06 mg/kg 20.03 mg/kg	3 0	5 5
Allen et al., 1978	Rats	$CuSO_4$ / Subchronic / Dietary / 63 days / Males	Altered levels of cholesterol, hematocrit, body weight, liver Cu burden, heart weight and heart weight to body weight ratio	0.57 µg 5 µg	3 0	10 10
Allen et al., 1988	Rats	NS / Subchronic / Dietary / 49 days / Males	Altered levels of renal, liver and arteriole GSH, liver SOD and liver GSH-PX	0.2 µg 10 µg	2 0	8 8
Allen et al., 1978	Rats	$CuSO_4$ / Chronic / Dietary / 168 days / Males	Altered cholesterol metabolism	0.57 µg/g 5 µg/g	2 0	10 10
Allen et al., 1996	Rats	$CuCO_3$ / Chronic / Dietary / 140 days / Males	Altered hematocrit, ceruloplasmin body weight, growth efficiency, growth potential index, liver weight, liver weight to body weight ratio, heart weight to body weight ratio, kidney weight to body weight ratio and Cu levels in the spleen, liver, kidney and cardiovascular system	5.79 mg/kg 0.46 mg/kg	0 3	5 5

Andersen et al., 2007	Rats	$CuSO_4$ / Subchronic / Dietary / 49 days / Females	Decreased serum copper and iron, decreased liver iron and copper	5 mg/kg 2.5 mg/kg 0.75 mg/kg	0 3 3	8 8 8
Arce et al., 1992	Mice	$CuSO_4$ / Subchronic / Dietary / 39 days / Females	Altered hematocrit, liver iron content and ceruloplasmin.	1 ppm 10 ppm	2 0	21 21
Auclair et al., 2006	Mice	$CuCO_3$ / Subchronic / Dietary / 84 days / Males	Decreased copper concentration, decreased plasma Cp activity, decreased hematocrit, decreased hemoglobin, altered mean cell volume, decreased mean cellular hemoglobin concentration	6 ppm 0.5 ppm	0 3	16 16
Baker et al., 1999	Humans	$CuSO_4$ / Subchronic / Dietary / 42 days / Males	Altered levels of urinary pyridinoline and deoxypyridinoline	1.6 mg/day 0.7 mg/day	0 2	11 11
Bala et al., 1992	Pig	NS / Subchronic / Dietary / 77 days / Males & Females	Altered heart weight, serum and liver copper burden and mononuclear cell reactivity.	0.8 mg/kg/day 6.4 mg/kg/day	3 0	6 6
Bala et al., 1990	Rats	$CuCO_3$ / Subchronic / Dietary / 35 days/ Males $CuCO_3$ / Subchronic / Dietary / 56 days / Males	Altered levels of heart weight to body weight ratio, immune functioning indicators and mitogen reactivity	0.6 µg/g 6 µg/g 0.6 µg/g 6 µg/g	3 0 2 0	13 13 13 13
Bode et al., 1992	Rats	$CuSO_4$ / Subacute / Dietary / 28 days / Males	Altered body weight; hematocrit; Cu burden in skeletal muscle, kidney, liver and serum; heart weight, cholesterol, ceruloplasmin, respiration rate in liver and kidney and liver acceptor control index	0.4 g/kg 5.2 g/kg	3 0	16 16

Bremmer et al., 1987	Rats	$CuSO_4$ / Subchronic / Dietary / 42 days / Males	Altered liver and serum Cu burden; gluthione peroxidase in liver, kidney MT-I and body weight.	0.15 mg/kg/day 10 mg/kg/day	3 0	8 8
Chen et al., 2002	Rats	NS / Subchronic / Dietary / 35 days / Males	Decreased body weight and heart weight, decreased heart weight to body weight ratio, decreased liver SOD activity, altered mitochondrial respiration in presence of NADH	7.19 mg/kg 0.78 mg/kg	0 3	7 8
Cockell et al., 2005	Rats	NS / Subacute / Dietary / 30 days / Males	Decreased liver copper, decreased total SOD, decreased plasma copper, decreased plasma iron, decreased plasma carbonyl	6 mg/kg 0.5 mg/kg	0 3	30 30
Cunnane et al., 1985	Rats	NS / Subchronic / Dietary / 84 days / Males	Altered liver and body weight; liver weight to body weight ratio; heart weight to body weight ratio; plasma Cu; phospholipid fatty acid composition in the plasma, liver and heart; and liver triglyceride fatty acid composition.	1 mg/kg/day 6 mg/kg/day	3 0	10 10
Davidson et al., 1992	Rats	$CuCO_3$ / Subchronic / Dietary / 35 days / Males	Altered body weight, heart weight, heart weight to body weight ratio, liver SOD, hematocrit, cardiovascular histopathology, heart rate and EKG variables	6.2 µmol/kg 92.4 µmol/kg	3 0	6 6
Davis et al., 2002	Rats	NS / Subacute / Dietary / 28	Decreased cp activity,	5.3 µg/g	0	9

		days / Males	decreased copper concentration in plasma and liver	0.8 µg/g	2	9
Davis et al., 2003	Humans	$CuSO_4$ / Subacute / Dietary / 42 days / Males	Decreased fecal copper concentration, increased in vitro production of hydroxyl radicals, increased intestinal phosphatase activity in fecal water	2.59 mg/d 0.59 mg/d	0 3	17 17
DiSilvestro et al., 1992	Rats	$CuSO_4$ / Subchronic / Dietary / 42 days / Males	Altered levels of plasma caeruloplasmin and liver copper burden in the two highest dose groups. Altered body weight, heart weight to body weight ratio, hemoglobin and plasma cholesterol in highest dose group	8 ppm 2.5 ppm 0.2 ppm	0 2 3	16 16 16
Dong et al., 2005	Rats	$CuSO_4$ / Subchronic / Dietary / 35 days / Males	Decreased liver & kidney copper, increased heart weight, increased contractility, altered IGF levels, decreased hematocrit, increased liver iron	6 mg/kg 0.5 mg/kg	0 4	10 10
Falcone et al., 2005	Rats	$CuSO_4$ / Chronic / Dietary / 180 days / Males	Decreased kidney copper	5.88 mg/kg 2.94 mg/kg 1.62 mg/kg	0 0 1	9 9 8
Fields et al., 1997	Rats	NS / Subacute / Dietary / 28 days / Males & Females	Altered body weight; liver weight to body weight; pancreas weight; liver and pancreatic Cu burden; lipid peroxidation; amylase activity, lipase and insulin in the pancreas; and plasma insulin levels	0.6 µg/g 6 µg/g	3 0	10 10

Giovanetti et al., 1998	Mice	$CuSO_4$ / Subacute / Dietary / 28 days / Males	Altered body weight; liver and respiratory system Cu burden and levels of Cu-Zn SOD and GSSG in the respiratory system	0.44 ppm 4.98 ppm	3 0	36 36
Gitlin et al., 1992	Rats	NS / Subacute / Dietary / 28 days / Males and Females	Altered levels of ceruloplasmin and serum Cu	0.6 mg/kg/day 6 mg/kg/day	2 0	4 4
Gobejishvili et al., 2002	Rats	$CuSO_4$ / Subacute / Dietary / 28 days / Males	Decreased hematocrit, decreased copper in liver, Reduce time to 50% relaxation induced by L-arginine	5.6 mg/kg 0.33 mg/kg	0 4	21 21
Goodman et al., 1973	Rats	$CuSO_4$ / Subchronic / Drinking Water / 60 days / Males	Altered heart weight, heart weight to body weight ratio and cardiovascular histopathology.	0 mg/L 40 mg/L	3 0	4 6
Gordon et al., 2005	Rats	$CuSO_4$ / Subacute / Dietary / 28 day / Males	Decreased liver copper, altered mean fluorescent intensity in neutrophils, altered size and shape of neutrophils	6.18 mg/kg 0.29 mg/kg	0 3	4 4
Hamilton et al., 2000	Mice	NS / Subchronic / Dietary / 98 days / Males	At the two lowest dose groups, altered heart weight; liver and kidney weight; liver and kidney copper, enzyme activities in the liver and kidney; aortic lesions; cholesterol and triglyceride levels; and ceruloplasmin oxidase activity	0.6 mg/kg/day 2 mg/kg/day 6 mg/kg/day	4 4 0	12 12 11
Harvey et al., 2003	Humans	$CuCl_2$ / Subacute / Dietary / 56 days / Males	Decreased loss of endogenous copper stores	6 mg/d 1.6 mg/d 0.7 mg/d	0 1 1	12 12 12
Hopkins et al., 1995	Rats	$CuCO_3$ / Chronic / Dietary / 161 days / Males and Females	Altered serum Cu burden; hemoglobin; mitogen and mononuclear cell activity in the	2.8 mg/kg/day 6.6 mg/kg/day	3 0	5 5

			spleen and neutrophil activity			
Johnson et al., 1993	Rats	NS / Subchronic / Dietary / 35 days / Males	Altered ceruloplasmin activity; plasma Cu burden; RBC SOD activity; liver Cu burden; liver cytochrome C oxidase activity and platelet cytochrome-C oxidase activity in the four lowest dose groups. Altered levels of Cu-Zn SOD in liver in the three lowest dose groups. Altered red cell distribution width, hematocrit and hemoglobin in the two lowest dose groups	0.2 µg/g 1 µg/g 2 µg/g 3 µg/g 4 µg/g	3 3 2 2 0	10 10 10 10 10
Johnson et al., 2004	Rats	$CuSO_4$ / Subacute / Dietary / 35 days / Males	Decreased liver copper, decreased liver iron, decreased body weight, decreased hemoglobin & hematocrit, decreased amine oxidase, lower CCO activity in mitochondria, increased HO-1 content in liver, increased HO-1 in heart	5.4 mg/kg 0.3 mg/kg	0 3	10 10
Johnson et al., 2005	Rats	$CuSO_4$ / Subchronic / Dietary / 42 days / Males	Decreased liver & kidney copper, decreased liver CCO, decreased Cp, increased hemoglobin, decreased et heart weight, decreased SOD	6 mg/kg 3 mg/kg 2.5 mg/kg 2 mg/kg 1.5 mg/kg 1 mg/kg 0.63 mg/kg	0 1 1 1 2 2 3	7 7 7 7 7 7 7
Kang et al., 2000	Mice	NS / Subchronic / Dietary / 35 days / Males & Females	Altered Cu-Zn SOD; ceruloplasmin; heart weight; body weight; Cu burden in the liver and cardiovascular system; and gene expression in the	0.35 mg/kg/day 6 mg/kg/day	3 0	10 10

			cardiovascular system			
Karimbakas et al., 1988	Mice	NS / Subacute / Dietary / 21 days / Males	Altered body weight; heart weight; spleen weight; thymus weight; ceruloplasmin; Cu burden; hemoglobin; hematocrit; RBC Cu-Zn SOD activity; neutrophil count, lymphocyte count, lung Cu-Zn SOD, Ly-6g levels in immune system and respiratory myelo-peroxidase activity	1.05 µg/g 6.4 µg/g	3 0	6 6
Kelley et al., 1995	Human	NA / Subacute / Dietary / 24 days / Males	Altered levels of lymphocytes	0.66 mg/day	2	11
Klaahsen et al., 2007	Rats	$CuCO_3$ / Subchronic / Dietary / 35 days / Males	Decreased final heart weight, decreased body weight and heart weight to body weight ratio, decreased hematocrit, decrease CU SOD in liver	6 mg/kg 0 mg/kg	0 3	4 4
Klevay et al., 1981	Rats	$CuSO_4$ / Subchronic / Dietary / 35 days / Males	Altered EKG variables, plasma cholesterol and longevity	0.79 µg/g 3.79 µg/g	6 0	20 20
Klevay et al., 1985	Mice	$CuSO_4$ / Chronic / Drinking Water / 100 days / Female	Altered heart rate and Pr interval	0 µg/ml 10 µg/ml	3 0	16 16
Klevay et al., 1986	Humans	NA / Subchronic / Dietary / 150 days / Males	Altered plasma glucose, insulin and plasma Cu levels	0.78 mg/day	3	5
Lai et al., 1994	Rats	$CuSO_4$ / Subacute / Drinking Water / 28 days / Males	Altered levels of liver and cardiovascular SOD activity; liver and cardiovascular SOD protein; and liver mRNA	0 µg/ml 3 µg/ml	2 0	10 10
Lai et al., 1995	Humans	NA / Subchronic / Drinking Water / 28 days / Males	Altered levels of hematocrit, body weight, liver Cu burden,	0 µg/ml 3 µg/ml	3 0	10 10

			plasma cholesterol, liver enzyme activity, cardiovascular enzyme activity, liver enzyme mRNA and liver protein concentration			
Lai et al., 1996	Rats	$CuSO_4$ / Subacute / Drinking Water / 28 days / Males	Altered hematocrit, body weight, heart weight, liver weight, Cu burden in the liver and liver enzyme activity	0 µg/ml 3 µg/ml	3 0	10 10
Li et al., 2005	Rats	NS / Chronic / Dietary / 470 days / Males	Decreased kidney and liver copper, progressive deterioration of heart, swelling and disorganization of mitochondria in myocardium, altered ECG	5.7 mg/kg 3.1 mg/kg 1.65 mg/kg	0 4 4	5 5 5
Li et al., 2005	Rats	$CuSO_4$ / Subacute / Dietary / 35 days / Males	Decreased liver copper, decreased heart copper, decreased body weight, decreased heart weight, decreased hematocrit, decreased liver iron	7.28 mg/kg 2.45 mg/kg 0.79 mg/kg 0.37 mg/kg	0 3 3 3	4 8 7 4
Mao et al., 1998	Rats	NS / Subchronic / Dietary / 77 days / Males	Altered body weight, heart weight, hematocrit, liver Cu burden and cardiovascular histopathology	1 mg/kg/day 7 mg/kg/day	3 0	4 4
Mao et al., 1999	Rats	$CuCO_3$ / Subchronic / Dietary / 84 days / Males	Altered liver SOD activity, altered cardiovascular EKG variable	2.7 mg/kg/day 6.2 mg/kg/day	3 0	5 5
Menino et al., 1986	Mice	$CuCO_3$ / Subchronic / Dietary / 60 days / Females	Altered hemoglobin, hematocrit, and body weight at the three lowest doses. Altered in vitro blastocyte formation,	11 ppm 6 ppm 5 ppm 4 ppm	0 0 0 0	15 19 19 20

			fertilization rate and heart weight at the two lowest doses	3 ppm 2 ppm 1 ppm	3 4 4	20 19 18
Olin et al., 1994	Rats	NS / Subacute / Dietary / 21 days / Males & Females	Altered red cell Se-GSHPx activity, RBC SOD activity, extracellular SOD, SE-GSHPx activity, ceruloplasmin, thyroid hormone levels, anti-oxidant defense, plasma Cu burden, brain Cu burden and liver Cu burden	7.9 nmol/g 125.9 nmol/g	3 0	28 36
Prohaska et al., 1982	Rats	$CuSO_4$ / Subchronic / Drinking Water / 35 days / Males	Altered body weight, heart weight, hematocrit, ceruloplasmin, Cu burden, norepinephrine levels, left ventricular pressure, and oxygen consumption	0 ppm 20ppm	3 0	11 10
Prohaska et al., 1994	Rats	$CuSO_4$ / Subacute / Dietary / 28 days / Males and Females	Altered brain weight, body weight, hemoglobin, ceruloplasmin, liver Cu burden, brain Cu burden, norepinephrine levels, dopamine levels, brain DBM activity and adrenal DBM activity	0.4 mg/kg/day 4 mg/kg/day	3 0	17 17
Prohaska et al., 1995	Rats	$CuSO_4$ / Subchronic / Drinking Water / 38.5 days / Males	Altered heart weight, Cu burden in the brain and liver, body weight, and liver iron	0 mg/L 20 mg/L	3 0	4 4
Prohaska et al., 2001	Rats	$CuSO_4$ / Subacute / Drinking Water / 30 days / Females	Altered body weight, liver Cu burden, brain Cu burden, adrenal dopamine enzyme activity, brain dopamine enzyme activity, adrenal Cu-Zn	20 mg/l/day 0 mg/l/day	0 3	6 6

			SOD, and brain Cu, Zn SOD			
Prohaska et al., 2003	Mice & Rats	$CuSO_4$ / Subchronic / Drinking water / 35 days / Females	Decreased liver copper, decreased liver SOD, decreased hematocrit	20 mg/L 0 mg/L 20 mg/L 0 mg/L	0 2 0 3	5 5 5 5
Rayssiguier et al., 1993	Rats	$CuCO_3$ / Subchronic / Dietary / 42 days / Males	Altered body weight, liver weight, heart weight, hematocrit, plasma Cu burden, plasma triglycerides, plasma lipids, plasma APO B, serum lipid peroxidation, cardiovascular lipid peroxidation and liver lipid peroxidation	0.6 mg/kg/day 7.5 mg/kg/day	3 0	12 12
Reeves et al., 2005	Rats	NS / Subacute / Dietary / 19 days / Males NS/ Subacute / Dietary / 19 days / Females	In both males and females decreased serum copper, decreased serum iron, decreased serum Cp activity, decreased serum SOD activity, altered soleus muscle CO1 activity, decreased hemoglobin, decreased MCV, decreased RDW, decreased iron absorption, decreased iron excretion, decreased iron transporter protein, decreased liver, kidney, duodenal and serum copper at deficient dose	5.0 mg/kg 0.25 mg/kg 5.0 mg/kg 0.25 mg/kg	0 3 0 3	8 8 8 8
Rock et al., 1995	Rats	$CuCO_3$ / Subchronic / Dietary / 42 days / Males	Altered body weight, heart weight, hematocrit, RBC SOD activity, plasma Cu burden, total cholesterol, RBC survival, RBC half-life, fluorenscence	0.6 mg/kg/day 7.5 mg/kg/day	3 0	10 10

			anisotropy, RBC hemolysis and RBC TBARS			
Saari et al., 1999	Rats	NS / Subchronic / Dietary / 35 days / Males	Altered liver and heart Cu burden and heart weight at the three lowest doses. Altered hematocrit, haemoglobin, and cardiac resistance, heart rate and stroke volume at the highest dose	6 ppm 0.8 ppm 0.4 ppm 0 ppm	0 3 3 3	5 5 5 5
Saari et al., 2002 (91)	Rats	$CuSO_4$ / Subchronic / Dietary / 35 days / Males	Altered Cu levels in the cardiovascular system and the liver in the three lowest dose groups. Altered bodyweight, heart weight and hematocrit in the lowest dose group	0 mg/kg/day 1.6 mg/kg/day 3.2 mg/kg/day 24 mg/kg/day	3 1 1 0	4 7 8 4
Saari et al., 2002	Rats	$CuSO_4$ / Subchronic / Dietary / 35 days / Males	Altered platelet count in the four lowest dose groups. Altered RBC distribution width in the two lowest dose groups. Altered haemoglobin, heart weight, neutrophil count and haemoglobin in the lowest dose group	0.27 mg/kg/day 1.43 mg/kg/day 2.92 mg/kg/day 4.27 mg/kg/day 6.15 mg/kg/day	3 2 2 0 0	13 13 13 13 13
Saari et al., 2007	Rats	$CuSO_4$ / Subchronic / Dietary / 35 days / Males	Decreased liver copper & iron, decreased body and heart weight, decreased hematocrit, increased cardiac iNOS, altered eNOS protein levels, eleated total cardiac NOS activity	6 mg/kg 0.3 mg/kg	0 3	25 25
Schuschke et al., 1995	Rats	NS / Subacute / Dietary / 7 days / Males /	Altered bleeding time and liver copper burden.	6 ppm 3 ppm 1.5 ppm	0 1 3	5 5 5

		NS / Subacute / Dietary / 21 days / Males	Altered bleeding time and liver copper burden.	6 ppm 3 ppm 1.5 ppm	0 1 3	7 6 5
		NS / Subacute / Dietary 35 days / Males	Altered bleeding time and liver copper burden.	6 ppm 3 ppm 1.5 ppm	0 3 3	5 6 6
Schuschke et al., 1999	Rats	$CuSO_4$ / Subacute / Dietary / 28 days / Males	Altered erythrocyte Cu, Zn-SOD activity, aortic Cu, Zn-SOD activity, hematocrit and mean arterial pressure in the three lowest doses	0 ppm 1.5 ppm 3 ppm 6 ppm	3 3 3 0	6 5 6 5
Schuschke et al., 2002	Rats	$CuSO_4$ / Subacute / Dietary / 28 days / Males	Decreased body weight, decreased liver copper, decreased heart weight to body weight ratio, greater MPO activity in lung and kidney	6.18 mg/kg 0.29 mg/kg	0 3	5 5
Smith et al., 2002	Rats	NS / Subchronic / Dietary / 49 days / Males	Decreased Cp, decreased copper and iron in liver, bone mineral density loss in femur	5.7 mg/kg 1.1 mg/kg	0 3	18 18
Sugawara et al., 1999	Rats	$CuCl_2$ / Subchronic / Dietary / 35 days / Males & Females	Altered liver, kidney, GI Cu burden and liver metallothionein	0.5 mg/kg/day 10 mg/kg/day	2 0	5 5
Turnlund et al., 1990	Humans	$CuSO_4$ / Subchronic / Dietary / 90 days / Males	No effects	0.785 mg/day 1.68 mg/day	1 0	11 11
Wang et al., 1996	Rats	$CuCO_3$ / Subchronic / Dietary / 42 days / Males	Altered body weight, liver weight heart weight and liver u burden.	9.4 µmol/kg 103.9 µmol/kg	3 0	8 8
Welch et al., 2007	Rats	NS / Subchronic / Dietary / 60 days / Males	Decreased p-phenylenediamine oxidase activity in serum, decreased serum Cp, decreased	10.5 mg/kg 0.43 mg/kg	0 3	5 5

			body weight, decreased liver copper and iron, iron deposits in spleen			
Wildman et al., 1995	Rats	NS / Chronic / Dietary / 154 days / Males	Altered cardiovascular histopathology at the two lowest doses. Altered liver Cu burden, ceruloplasmin, serum Cu burden at the lowest dose	1.3 mg/kg/day 2.8 mg/kg/day 6.7 mg/kg/day	3 3 0	6 6 6
Zeng et al., 2007	Rats	$CuSO_4$ / Subchronic / Dietary / 35 days / Males	Decreased body weight, decreased heart to body weight ratio, decreased hemoglobin and hematocrit, decreased copper in heart and liver, perturbed mitochondrial function, decreased protein expression of COX I, Vb, V1b	6.26 mg/kg 0.16 mg/kg	0 3	10 10

References

Ajayi, O.B. 2005. Micronutrient changes in some tissues of copper deficient rats. *Pakistan J. Nutr.* 4:123-125.

Alissa, E.M., Bahijri, S.M., Lamb, D.J., Ferns, G.A.A. 2004. The effects of co-administration of dietary copper and zinc supplements on atherosclerosis, antioxidant enzymes and indices of lipid peroxidation in the cholesterol-fed rabbit. *Int. J. Exp. Path.* 85:265-275.

Allen, C.B. 1996. Effects of dietary copper deficiency on relative food intake and growth efficiency in rats. *Physiol. Behav.* 59:247-253.

Allen, K.G.D., Arthur, J.R., Morrice, P.C., Nicol, F., Mills, C.F. 1988. Copper deficiency and tissue glutathione concentration in the rat. *Proc. Soc. Exp. Biol. Med.* 187:38-43.

Allen, K.G.D. Klevay, L.M. 1978. Copper deficiency and cholesterol metabolism in the rat. *Atherosclerosis*, 31:259-271.

Andersen, H.S., Gambling, L., Holtrop, G. McArdle, H.J. 2007. Effect of dietary copper deficiency on iron metabolism in the pregnant rat. *Br. J. Nutr.* 97:239-246.

Araya, M., Chen, B., Klevay, L.M., Strain, J.J., Johnson, L., Robson, P., et al. 2003a. Confirmation of an acute no-observed-adverse-effect level (NOAEL) and low-observed-adverse-effect level (LOAEL) for copper in bottled drinking water in a multi-site international study. *Regul. Toxicol. Pharmacol.* 38:389-399.

Araya, M., McGoldrick, M.C., Klevay, L.M., Strain, J.J., Robson, P., Nielsen, F., et al. 2001. Determination of an acute no-observed-adverse-effect level (NOAEL) for copper in water. *Reg. Toxicol. Pharmacol.* 34:137-145.

Araya, M., Olivares, M., Pizarro, F. González, M., Speisky, H., Uauy, R. et. al. 2003c. Gastrointestinal symptoms and blood indicators of copper load in apparently healthy adults undergoing controlled copper exposure. *Am. J. Clin. Nutr.* 77:646-650.

Araya, M., Olivares, M., Pizarro, F., Llanos, A., Figueroa, G. Uauy, R. 2004. Community-based randomized double-blind study of gastrointestinal effects and copper exposure in drinking water. *Environ. Health. Perspect.* 112:1068-1073.

Araya, A., Pena, C., Pizarro, F., Olivares, M. 2003b. Gastric response to acute copper exposure. *Sci. Total. Environ.* 303:253-257.

Araya, M., Olivares, M., Pizarro, F. González, M., Speisky, H., Uauy, R. et. al. 2003c. Gastrointestinal symptoms and blood indicators of copper load in apparently healthy adults undergoing controlled copper exposure. *Am. J. Clin. Nutr.* 77:646-650.

Arce, D.S., Keen, C.L. 1992. Reversible and persistent consequences of copper deficiency in developing mice. *Reprod. Toxicol.* 6:211-221.

Armstrong, T.A., Cook, D.R., Ward, M.M., Williams, C.M., Spears, J.W. 2004. Effect of dietary copper source (cupric citrate and cupric sulphate) and concentration on growth performance and fecal copper excretion in weanling pigs. *J. Anim. Sci.* 82:1234-1240.

Auclair, S., Feillet-Coudray, C., Coudray, C., Schneider, S., Muckenthaler, M.U., Mazur, A. 2006. Mild copper deficiency alters gene expression of proteins involved in iron metabolism. *Blood Cell Mol. Dis.* 36:15-20.

Baker, A., Harvey, L., Majask-Newman, G., Fairweather-Tait, S., Flynn, A., Cashman, K. 1999a. Effect of dietary copper intakes on biochemical markers of bone metabolism in healthy adult males. *European J. Clin. Nutr.* 53:408-412.

Baker, A., Turkey, E., Bonham, M.P., O'Connor, J.M., Strain, J.J., Flynn, A., Cashman, K.D. 1999b. No Effect of copper supplementation on biochemical markers of bone metabolism in healthy adults. *Brit. J. Clin. Nutr.* 82:283-290.

Bala, S., Failla, M.L., Lunney, J. 1990. T-cell numbers and mitogenic responsiveness of peripheral blood mononuclear cells are decreased in copper deficient rats. *Nutr. Res.* 10:749-760.

Bala, S., Lunney, J.K., Failla, M.L. 1992. Effect of copper deficiency on T-cell mitogenic responsiveness and phenotypic profile of blood mononuclear cells from swine. *Am. J. Vet. Res.* 53:1231-5.

Becaria, A., Lahiri, D.K., Bondy, S.C., Chen, D., Hamadeh, A., Li, H. 2006. Aluminum and copper in drinking water enhance inflammatory or oxidative events specifically in the brain. *J. Neuroimmun.* 176:16-23.

Bode, A.M., Miller, L.M., Faber, J., Saari, J.T. 1992. Mitochondrial respiration in heart, liver, and kidney of copper-deficient rats. *J. Nutr. Biochem.* 3:668-672.

Bremner, I., Morrison, J.N., Wood, A.M., Arthur, J.R. 1987. Effects of changes in dietary zinc, copper and selenium supply and of endotoxin administration on metallothionein I concentrations in blood cells and urine in the rat. *J. Nutr.* 117:1595-1602.

Canadian Council on Animal Care. 1984. *Guide to the Care and Use of Experimental Animals. Volume 2.* http://www.ccac.ca/en/CCAC_Programs/Guidelines_Policies/GDLINES/Guidelis.htm.

Chen, X., Jennings, D.B., Medeiros, D.M. 2002. Impaired cardiac mitochondrial membrane potential and respiration in copper-deficient rats. *J. Bioenergetics Biomem.* 34:397-406.

Cisternas, F.A., Tapia, G., Arredondo, M., et al. 2005. Early histological and functional effects of chronic copper exposure in rat liver. *BioMetals* 18:541-551.

Cockell, K.A., Belonje, B. 2002. The carbonyl content of specific plasma proteins is decreased by dietary copper deficiency in rats. *J. Nutr.* 132:2514-2518.

Cockell, K.A., Wotherspoon, A.T.L., Belonji, B., Fritz, M.E., Madère, R., Hidiroglou, N. et al. 2005. Limited effects of combined dietary copper deficiency/iron overload on oxidative stress parameters in rat liver and plasma. *J. Nutr. Biochem.* 16:750-756.

Cromwell, G.L. Stahly, T.S., Monegue, H.J. 1989. Effects of source and level of copper on performance and liver copper stores in weanling pigs. *J. Anim. Sci.* 67:2996-3001.

Cunnane, S.C., Horrobin, D.F., and Manky, M.S. 1985. Contrasting effects of low or high copper intake on rat tissue lipid essential fatty acid composition. *Ann. Nutr. Metab.* 29:103-110.

Davidson, A., Medeiros, D.M., and Hamlin, R.L. 1992. Cardiac ultrastructural and electrophysiological abnormalities in postweanling copper-restricted and copper-repleted rats in the absence of hypertrophy. *J. Nutr.* 122:1566-1575.

Davis, C.D., Johnson, W.T. 2002. Dietary copper affects azoxymethane-induced intestinal tumor formation and protein kinase C isozyme protein and mRNA expression in colon of rats. *J. Nutr.* 132:1018-1025.

Davis, C.D. 2003. Low dietary copper increases fecal free radical production, fecal water alkaline phosphatase activity and cytotoxicity in healthy men. *J. Nutr.* 133:522.

DiSilvestro, R.A., Medeiros, D.M. 1992. Low and marginal copper intake by postweanling rats: Effects on copper status and resistance to carbon tetrachloride hepatotoxicity. *Metabolism.* 41:1122-1124.

Dong, F., Esberg, L.B., Roughead, Z.K., Ren, J., Saari, J.T. 2005. Increased contractility of cardiomyocytes from copper-deficient rats is associated with up-regulation of cardiac IFG-I receptor. *Am. J. Physiol. Heart Circ. Physiol.* 289:H78-H84.

Falcone, J.C., Saari, J.T., Kang, Y.J., Schuschke, D.A. 2005. Vasoreactivity in an adult rat model of marginal copper deficiency. *Nutr. Res.* 25:177-186.

Feng, J., May, W.Q., Gu, Z.L. 2007. Effects of dietary copper (II) sulfate and copper proteinate on performance and blood indexes of copper status in growing pigs. *Biol. Trace Elem. Res.* 120:171-178.

Fields, M., Lewis, C.G. 1997. Impaired endocrine and exocrine pancreatic functions in copper-deficient rats: The effect of gender. *J. Am. Col. Nutr.* 16:346-351.

Food and Nutrition Board, Institute of Medicine. 2001. Dietary reference intakes: vitamin A, vitamin K, arsenic, boron, chromium, copper, iodine, iron, manganese, molybdenum, nickel, silicon, vanadium, and zinc. Washington DC: National Academy Press.

Fuentealba, I.C., Haywood, S., Trafford, J. 1989. Variations in the intralobular distribution of copper in the livers of copper-loaded rats in relation to the pathogenesis of copper storage diseases. *J. Comp. Path.* 100:1-11.

Fuentealba, I.C., Mullins, J.E., Aburto, E.M., Lau, J.C., Cherian, G.M. 2000. Effect of age and sex on liver damage due to excess dietary copper in Fischer 344 rats. *Clin. Toxicol.* 38:709-717.

Gitlin, J.D., Schroeder, J.J., Lee-Ambrose, L.M. 1992. Mechanisms of caeruloplasmin biosynthesis in normal and copper-deficient rats. *Biochem. J.* 282:835-839.

Giovanetti, A., Rossi, L., Mancuso, M., Lombardi, C.C., Marasco, M.R., Manna, F., et al. 1998. Analysis of lung damage induced by trichloroethylene inhalation in mice fed diets with low, normal and high copper content. *Tox. Path.* 26:628-635.

Gobejishvili, L., Saari, J.T., Adeagbo, A.S.O., Zhang, X., Schuschke, D.A. 2002. Dietary copper deficiency increases inducible nitric oxide synthase-mediated vascular dilation in rat aorta. *J. Trace Elem. Exp. Med.* 15:85-95.

Goldschmith, A., Infante, C., Leiva, J., Motles, E., Palestini, M. 2005. Interference of chronically ingested copper in long-term potentiation (LTP) of rat hippocampus. *Brain Res.* 1056:176-182.

Gomi, F., Matsuo, M. 1995. Effect of copper deficiency on the activity levels of ceruloplasmin and superoxide dismutase in tissues of young and old rats. *Aging (Milano).* 7:61-66.

Goodman, J.R., Warshaw, J.B., Dallman, P.R. 1970. Cardiac hypertrophy in rats with iron and copper deficiency: Quantitative contribution of mitochondrial enlargement. *Pediat. Res.* 4:244-256.

Gordon, S.A., Lominadze, D., Saari, J.T., Lentsch, A.B., Schuschke, D.A. 2005. Impaired deformability of copper-deficient neutrophils. *Exp. Biol. Med.* 230:543-548.

Gotteland, M., Araya, M., Pizarro, F., Olivares, M. 2001. Effect of acute copper exposure on gastrointestinal permeability in healthy volunteers. *Dig. Dis Sci.* 46:1909-1914.

Greene, F.L., Lamb, L.S., Barwick, M., Pappas, N.J. 1987. Effect of dietary copper on colonic tumor production and aortic integrity in the rat. *J. Surg. Res.* 42:503-512.

Gross, J.B., Myers, B.M., Kost, L.J., Kuntz, S.M., LaRusso, N.F. 1989. Biliary copper excretion by hepatocyte lysosomes in the rat. Major excretory pathway in experimental copper overload. *J. Clin. Invest.* 83:30-39.

Gurel, Z., Ozcelik, D., Dursun, S. 2007. Apoptotic rate and metallothionein levels in the tissues of cadmium and copper-exposed rats. *Bio. Trace Elem. Res.* 116:203-217.

Hamilton, I.M.J., Gilmore, W.S., and Strain, J.J. 2000. Marginal copper deficiency and atherosclerosis. *J. Biol. Trace Element Res.* 78:179-189.

Harvey, L.J., Majsak-Newman, G., Dainty, J.R., Lewis, D.J., Langford, N.J., Crews, H.M. et al. 2003 Adaptive responses in men fed low- and high-copper diets. *British J. Nutr.* 90:161-168.

Haywood, S. 1985. Copper toxicosis and tolerance in the rat – changes in copper content of the liver and kidney. *J. Path.* 145:149-158.

Haywood, S., Comerford, B. 1980. The effect of excess dietary copper on plasma enzyme activity and on the copper content of the blood of the male rat. *J. Comp. Path.* 90:233-238.

Hebert, C.D. 1993. NTP Technical Report on toxicity studies of cupric sulfate (CAS No. 7758-99-8) administered in drinking water and feed to F344/N rats and B6C3F1 mice. *Toxicity Rept. Series.* NTIS PB95-120870/HDM:1-122.

Hopkins, R.G., Failla, M.L. 1995. Chronic intake of a marginally low copper diet impairs in vitro activities of lymphocytes and neutrophils for male rats despite minimal impact on conventional indicators of copper status. *J. Nutr.* 125:2658-2668.

Jantsch, W., Kulig, K., Rumack, B.H. 1985. Massive copper sulfate ingestion resulting in hepatotoxicity. *Clinc. Toxicol.* 22:585-588.

Johnson, W.T., DeMars, L.C.S. 2004. Increased heme oxygenase-1 expression during copper deficiency in rats results from increased mitochondrial generation of hydrogen peroxide. *J. Nutr.* 134:1328-1333.

Johnson, W.T., Dufault, S.N. Thomas, A.C. 1993. Platelet cytochrome c oxidase is an indicator of copper status in rats. *Nutr. Res.* 13:1153-1162.

Johnson, W.T., Johnson, L.A.K., Lukaski, H.C. 2005. Serum superoxide dismutase 3 (extracellular superoxide dismutase) activity is a sensitive indicator of Cu status in rats. *J. Nutr. Biochem.* 16:682-692.

Jones, A.A., Disilvestro, R.A., Coleman, M., and Wagner, T.L. 1997. Copper Supplementation of Adult Men: Effects on Blood Copper Enzyme Activities and Indicators of Cardiovascular Disease Risk. *Metabolism.* 46:1380-1383.

Kang, Y.J., Wu, H., Saari, J.T. 2000. Alterations in hypertrophic gene expression by dietary copper restriction in mouse heart. *Proc. Soc. Exp. Biol. Med.* 223:282-7.

Karimbakas, J., Langkamp-Henken, B., Percival, S.S. 1998. Arrested maturation of granulocytes in copper deficient mice. *J. Nutr.* 128:1855-1860.

Kelley, D.S., Daudu, P.A., Taylor, P.C., Mackey, B.E., Turnlund, J.R. 1995. Effects of low-copper diets on human immune response. *Am. J. Clin. Nutr.* 62:412-416.

Klaahsen, D., Ricklefs, K., Medeiros, D.M. 2007. Differential expression of genes involved with apoptosis, cell cycle, connective tissue proteins, fuel substrate utilization, inflammation and mitochondrial biogenesis in copper-deficient rat hearts: implication of a role for NfKb1. *J. Nutr. Biochem.* 18:719-726.

Klevay, L.M. 1985. Atrial thrombosis, abnormal electrocardiograms and sudden death in mice due to copper deficiency. *Atherosclerosis.* 54:213-224.

Klevay, L.M., Canfield, W.K., Gallagher, S.K. 1986. Decreased glucose tolerance in two men during experimental copper depletion. *Nutr. Rep. Int.* 33:371-382.

Klevay, L.M., Viestenz, K.E. 1981. Abnormal electrocardiograms in rats deficient in copper. *Am. J. Physiol.* 240:H185-H189.

Kvietkauskaite, R., Dringeliene, A., Markevicius, A., Siaurys, A., Acaite, J. 2004. Effect of low copper exposure on the antioxidant system and some immune parameters. *Vet. Human. Toxicol.* 46:169-172.

Lai, C.C., Huang, W.H., Askari, A., Klevay, L.M., Chiu, T.H. 1995. Expression of glutathione peroxidase and catalase in copper-deficient rat liver and heart. *Nutr. Biochem.* 6:256-262.

Lai, C.C., Huang, W.H., Askari, A., Wang, Y., Sarvazyan, N., Klevay, L.M., et al. 1994. Differential regulation of superoxide dismutase in copper-deficient rat organs. Free Radic. Biol. Med. 16:613-620.

Lai, C.C., Huang, W.H., Klevay, L.M., Chiu, T.H. 1996. Antioxidant enzyme gene transcription in copper-deficient rat liver. *Free Radic. Biol. Med.* 21:233-40.

Lai, Y.L., Yamaguchi, M. 2005. Effects of copper on bone component in the femoral tissues of rats: anabolic effect of zinc is weakened by copper. *Biol. Pharm. Bull.* 28:2296-2301.

Li, Y., Wang, L., Schuschke, D.A., Zhanxiang, Z., Saari, J.T., Kang, Y.J. 2005 Marginal dietary copper restriction induces cardiomyopathy in rats. *J. Nutr.* 135:2130-2136.

Liu, C.C.F., Medeiros, D.M. 1986. Excess diet copper increases systolic blood pressure in rats. *Bio. Trace Element Res.* 9:15-24.

Lucca, J.J.D., Saari, J.T., Falcone, J.C. Schuschke, D.A. 2002. Neointima formation in the rat carotid artery is exacerbated by dietary copper deficiency. *Exp. Biol. Med.* 227:487-491.

Lynch, S.M., Klevay, L.M. 1994. Contrasting effects of a dietary copper deficiency in male and female mice. *Proc. Soc. Exp. Biol. Med.* 205:190-196.

Massie, H.R., Aiello, V.R. 1984. Excessive intake of copper: Influence on longevity and cadmium accumulation in mice. *Mech. Ageing Dev.* 26:95-203.

Mao, S. 1999. Marginal copper and high fat diet produces alterations in electrocardiograms and cardiac ultrastructure in male rats. *Nutrition* 15:890-898.

Mao, S., Medeiros, D.M., Wildman, R.E.C. 1998. Cardiac hypertrophy in copper-deficient rats is owing to increased mitochondria. *Biol. Trace Element Res.* 64:175-184.

Menino, A.R., Damron, W.S., Henry, T.E., O'Claray, J.L. 1986. The influence of dietary copper on reproduction, growth and the cardiovascular system in Swiss-Webster female mice. *Lab. Ani. Sci.* 36:164-167.

Mullins, J.E., Fuentealba, I.C. 1998. Immunohistochemical detection of metallothionein in liver, duodenum and kidney and dietary copper-overload in rats. *Histol. Histopathol.* 13:627-633.

Murthy, R.C., Lal, S., Saxena, D.K., Shukla, G.S., Ali, M.M., and Chandra, S.V. 1981. Effect of manganese and copper interaction on behavior and biogenic amines in rats fed a 10% casein diet. *Chem. Biol. Interact*. 37:299-308.

Nelson, S.K., Huang, C-J., Mathias, M.M., and Allen, K.G.D. 1992. Copper-marginal and copper-deficient diets decrease aortic prostacyclin production and copper-dependent superoxide dismutase activity, and increase aortic lipid peroxidation in rats. *J. Nutr.* 122:2101-2108.

O'Connor, J.M., Bonham, M.P., Turley, E., McKeown, A., McKelvey-Martin, V.J., Gilmore, W.S., et al. 2003. Copper supplementation has no effect on markers of DNA damage and liver function in healthy adults (FOODCUE Project). *Ann. Nutr. Metab.* 47:201-206.

O'Donohue, J.W., Reid, M., Varghese, A., Portman, B., Williams, R. 1999. A case of adult chronic copper self-intoxication resulting in cirrhosis. *Eur. J. Med. Res.* 4:252.

Olin, K.L., Walter, R.M., and Keen, C.L. 1994. Copper deficiency affects selenoglutathione peroxidase and selenodeiodinase activities and antioxidant defense in weanling rats. *Am. J. Clin. Nutr. Vol*: 59:654-658. .

Ozcelik, D., Toplan, S., Ozdemir, S., Akyolcu, M.C. 2002. Effects of Excessive copper intake on haematological and hemorheological parameters. *Bio. Trace Elem. Res.* 89:35-42.

Pizarro, F., Olivares, M., Uauy, R., Contreras, P., Rebelo, A., and Gidi, V. 1999a. Acute gastrointestinal effects of graded levels of copper in drinking water. *Env. Health Persp.* 107:117-121.

Poiley SM, 1972. Growth Tables for 66 Strains and Stocks of Laboratory Animals. *Lab. Ani. Sci.* 22:759.

Pratt, W.B., Omdahl, J.L., and Sorenson, J.R. 1985. Lack of effects of copper gluconate supplementation. *Am. J. Clin. Nutr.* 42:681-682.

Prohaska, J.R., Bailey, W.R. 1994. Regional specificity in alterations of rat brain copper and catecholamines following perinatal copper deficiency. *J. Neurochem.* 63:1551-1557.

Prohaska, J.R., Bailey, W.R., and Lear, P.M. 1995. Copper deficiency alters rat peptidylglycine alpha-amidating monooxygenase activity. *J. Nutrition.* 125:1447-1454.

Prohaska, J.R., Brokate, B. 2001. Dietary copper deficiency alters protein levels of rat dopamine b-monooxygenase and tyrosine monooxygenase. *Exp. Biol. Med.* 226:199-207.

Prohaska, J.R., Geissler, J., Brokate, B., Broderius, M. 2003. Copper, zinc-superoxide dismutase protein but not mRNA is lower in copper-deficient mice and mice lacking the copper chaperone for superoxide dismutase. *Exp. Biol. Med.* 228:959-966.

Prohaska, J.R., Heller, L.J. 1982. Mechanical Properties of the Copper-deficient rat heart. *J. Nutr.* 12:2142-2150.

Rana, S.V.S., Kumar, A. 1980. Biological, haematological and histological observations in copper poisoned rats. *Ind. Health.* 18:9-17.

Rayssiguier, Y., Gueux, E., Bussiere, L., Mazur, A. 1993. Copper deficiency increases the susceptibility of lipoproteins and tissues to peroxidation in rats. *J. Nutr.* 123:1343-1348.

Reeves, P.G., DeMars, L.C.S., Johnson, W.T., Lukaski, H.C. 2005. Dietary copper deficiency reduces iron absorption and duodenal enterocyte hephaestin protein in male and female rats. *J. Nutr. 135:92-96.*

Reiser, S., Powell, A., Yang, C.-Y., Canary, J.J. 1987. Effect of copper intake on blood cholesterol and its lipoprotein distribution in men. *Nutr. Reports Intl.* 36:641-649.

Rock, E., Gueux, E., Mazur, A., Motta, C., Rayssiguier, Y. 1995. Anemia in copper-deficient rats: role of alterations in erythrocyte membrane fluidity and oxidative damage. *Am. J. Physiol.* 269:C1245-C1249.

Saari, J.T. 2002a. Dietary copper deficiency reduces the elevation of blood pressure caused by nitric oxide synthase inhibition in rats. *Pharm.* 65:141-144.

Saari, J.T. 2002b. Renal copper as an index of copper status in marginal deficiency. *Biol. Trace. Elem. Res.* 86:237-247.

Saari, J.T., Stinnett, H.O., Dahlen, G.M. 1999. Cardiovascular measurements relevant to heart size in copper-deficient rats. *J. Trace Elem. Med. Biol.* 13:27-33.

Saari, J.T., Wold, L.E., Duan, J., Ren, J., Carlson, H.L., Bode, A.M. 2007. Cardiac nitric oxide synthases are elevated in dietary copper deficiency. *J. Nutr. Biochem.* 18:443-448.

Schuschke, D.A., Percival, S.S., Lominadze, D., Saari, J.T., Lentsch, A.B. 2002. Tissue-specific ICAM-1 expression and neutrophil transmigration in the copper-deficient rat. *Inflammation* 26:297-303.

Schuschke, D.A., Percival, S.S., Saari, J.T., and Miller, F.N. 1999. Relationship between dietary copper concentration and acetylcholine-induced vasodilation in the microcirculation of rats. *BioFactors* 10:321-327.

Schuschke, L.A., Saari, J.T., Miller, F.N., Schuschke, D.A. 1995. Hemostatic mechanisms in marginally copper-deficient rats. *J. Lab. Clin. Med.* 125:748-753.

Smith, B.J., King, J.B., Lucas, E.A., Akhter, M.P., Arjmandi, B.H., Stoechker, B.J. 2002. Skeletal uploading and dietary copper depletion are detrimental to bone quality of mature rats. *J. Nutr.* 132:190-196.

Sugawara, N., Sugawara, C. 1999. An iron-deficient diet stimulates the onset of the hepatitis due to hepatic copper deposition in the Long-Evans Cinnamon (LEC) rat. *Arch. Toxicol.* 73:353-8.

Turnlund, J.R., Jacob, R.A., Keen, C.L. Strain, J.J., Kelley, D.S., Domek, J.M., et al. 2004. Long-term high copper intake: effects on indexes of copper status, antioxidant status, and immune function in young men. *Am. J. Clin. Nutr.* 79:1037-44.

Turnlund, J.R., Keen, C.L., Smith, R.G. 1990. Copper status and urinary and salivary copper in young men at three levels of dietary copper. *Am. J. Clin. Nutr.* 51:658-664.

Wang, Y.R., WU, J.Y., Reaves, S.K., Lei, K.Y. 1996. Enhanced expression of hepatic genes in copper-deficient rats detected by the messenger RNA differential display method. *J. Nutr.* 126:1772-81.

Welch, K.D., Hall, J.O., Davis, T.Z. Aust, S.D. 2007. The effect of copper deficiency on the formation of hemosiderin in sprague-dawley rats. *Biometals. 20:829-839.*

Wildman, R.E.C., Hopkins, R., Failla, M.L., Medeiros, D.M. 1995. Marginal copper-restricted diets produce altered cardiac ultrastructure in the rat. *Proc. Soc. Exp. Biol. Med.* 210:43-49.

Zeng, H., Saari, J.T., Johnson, W.T. 2007. Copper deficiency decreases complex IV but not complex I, II, III, or V in the mitochondrial respiratory chain in rat heart. *J. Nutr.* 137:14.

Zhang, S.S., Noordin, M.M., Rahman, S.O. Haron, J. 2000. Effects of copper overload on hepatic lipid peroxidation and antioxidant defense in rats. *Vet. Hum. Toxicol.* 42:261-4.