Appendix Q

Additional UDP Simulation Modeling Results

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Appendix Q-1

UDP Results for the RC Millimole Regression – Starting at Estimated LD50 - 5000 mg/kg Upper Limit

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UDP Results for the RC Millimole Regression
Starting at Estimated LD50
5000 mg/kg Upper Limit
Results for 46 chemicals for the 3T3 NRU and 47 chemicals for the NHK NRU
(see notes to Table 6-4 for chemicals excluded)

Summary of Animals Used by Cell Type

Cell	Sigma	Method	Std. Error	Animals	Difference	P-Value*	% Change
3T3	0.12	Cyto	0.309	7.00	1.14	0.0034	14.0%
		Default	0.253	8.13			
	0.25	Cyto	0.293	7.77	1.22	0.0011	13.5%
		Default	0.249	8.99			
	0.5	Cyto	0.243	8.54	1.25	<.0001	12.7%
		Default	0.208	9.79			
	1.25	Cyto	0.210	9.13	1.23	<.0001	11.8%
		Default	0.165	10.36			
	2	Cyto	0.185	9.28	1.05	<.0001	10.2%
		Default	0.131	10.33			
		Average Animal Difference:			1.18		
NHK	0.12	Cyto	0.320	7.13	1.00	0.0045	12.3%
		Default	0.248	8.12			
	0.25	Cyto	0.303	7.88	1.07	0.0015	12.0%
		Default	0.241	8.96			
	0.5	Cyto	0.254	8.66	1.11	0.0001	11.4%
		Default	0.199	9.77			
	1.25	Cyto	0.214	9.25	1.14	<.0001	11.0%
		Default	0.154	10.39			
	2	Cyto	0.191	9.40	0.93	<.0001	9.0%
		Default	0.123	10.33			
		Average Animal Difference:			1.05		

Summary of Animal Deaths by Cell Type

Cell Type	Sigma	Method	3 Animals at Limit Dose	5 Reversals	Likelihood Ratio	Max Animals	Animals	Died	Percent Dead
3T3	0.12	Cyto	23.8%	54.6%	18.9%	2.6%	7.00	3.36	46.5%
		Default	23.3%	51.6%	21.5%	3.6%	8.13	3.44	43.7%
	0.25	Cyto	23.2%	31.7%	40.6%	4.6%	7.77	3.72	46.6%
		Default	22.5%	31.8%	38.2%	7.6%	8.99	3.80	43.8%
	0.5	Cyto	20.9%	18.3%	53.2%	7.6%	8.54	4.11	47.1%
		Default	19.6%	19.1%	47.7%	13.6%	9.79	4.18	44.3%
	1.25	Cyto	15.1%	12.7%	60.5%	11.7%	9.13	4.51	48.3%
		Default	13.3%	13.3%	53.0%	20.4%	10.36	4.63	45.9%
	2	Cyto	13.0%	11.7%	62.3%	13.0%	9.28	4.62	48.8%
		Default	10.5%	12.4%	56.4%	20.8%	10.33	4.74	46.9%
NHK	0.12	Cyto	25.4%	49.3%	22.2%	3.1%	7.13	3.34	46.4%
		Default	25.0%	50.7%	20.8%	3.5%	8.12	3.39	43.2%
	0.25	Cyto	24.5%	29.9%	40.3%	5.3%	7.88	3.69	46.5%
		Default	23.9%	31.5%	37.2%	7.4%	8.96	3.73	43.4%
	0.5	Cyto	22.0%	18.1%	51.6%	8.3%	8.66	4.09	47.0%
		Default	21.0%	18.8%	46.8%	13.3%	9.77	4.12	43.9%
	1.25	Cyto	15.5%	12.5%	59.7%	12.2%	9.25	4.51	48.3%
		Default	13.9%	13.2%	52.4%	20.5%	10.39	4.60	45.7%
	2	Cyto	12.6%	11.9%	61.9%	13.6%	9.40	4.63	48.9%
		Default	10.9%	12.3%	56.0%	20.8%	10.33	4.71	46.7%

Summary of Animals Used by GHS Toxicity Category and Cell Type

Toxcat	Cell	Sigma	Method	Std. Error	Animals	Difference	P-Value*	% Change
1	3T3	0.12	Cyto	0.639	10.42	0.20	0.4501	1.9%
			Default	0.491	10.61			
		0.25	Cyto	0.647	11.01	0.24	0.5000	2.1%
			Default	0.332	11.25			
		0.5	Cyto	0.582	11.37	0.39	0.4501	3.3%
			Default	0.193	11.75			
		1.25	Cyto	0.529	11.64	0.40	0.4011	3.3%
			Default	0.125	12.04			
		2	Cyto	0.456	11.48	0.35	0.4501	3.0%
			Default	0.122	11.83			
			Average Animal Difference:			0.31		
	NHK	0.12	Cyto	0.544	11.24	-0.67	0.3089	-6.4%
			Default	0.529	10.57			
		0.25	Cyto	0.460	11.84	-0.81	0.1354	-7.3%
			Default	0.412	11.03			
		0.5	Cyto	0.422	12.21	-0.64	0.0603	-5.5%
			Default	0.269	11.57			
		1.25	Cyto	0.407	12.39	-0.42	0.1118	-3.5%
			Default	0.159	11.97			
		2	Cyto	0.392	12.17	-0.45	0.0746	-3.9%
			Default	0.126	11.71			
			Average Animal Difference:			-0.60		
2	3T3	0.12	Cyto	0.722	8.11	-0.07	0.3429	-0.9%
			Default	0.240	8.05			
		0.25	Cyto	0.763	8.83	-0.39	0.5000	-4.6%
			Default	0.112	8.44			
		0.5	Cyto	0.800	9.37	-0.41	0.5000	-4.6%
			Default	0.159	8.96			
		1.25	Cyto	0.762	9.85	-0.44	0.4196	-4.6%
			Default	0.136	9.42			
		2	Cyto	0.605	10.03	-0.43	0.5000	-4.5%
			Default	0.088	9.60			
			Average Animal Difference:			-0.35		
	NHK	0.12	Cyto	0.233	7.31	0.88	**0.0464**	10.7%
			Default	0.318	8.18			
		0.25	Cyto	0.225	7.92	0.78	**0.0464**	8.9%
			Default	0.183	8.70			
		0.5	Cyto	0.300	8.33	0.96	0.0645	10.3%
			Default	0.242	9.28			
		1.25	Cyto	0.226	8.79	0.96	**0.0331**	9.9%
			Default	0.212	9.75			
		2	Cyto	0.140	9.19	0.57	**0.0464**	5.9%
			Default	0.112	9.77			
			Average Animal Difference:			0.83		

Summary of Animals Used by GHS Toxicity Category and Cell Type

Toxcat	Cell	Sigma	Method	Std. Error	Animals	Difference	P-Value*	% Change
3	3T3	0.12	Cyto	0.267	6.45	0.27	0.5000	4.1%
			Default	0.385	6.72			
		0.25	Cyto	0.264	7.00	0.06	0.4073	0.8%
			Default	0.309	7.06			
		0.5	Cyto	0.177	7.69	0.06	0.4688	0.8%
			Default	0.207	7.75			
		1.25	Cyto	0.096	8.67	0.02	0.4073	0.2%
			Default	0.087	8.69			
		2	Cyto	0.053	9.16	-0.03	0.3483	-0.4%
			Default	0.066	9.13			
			Average Animal Difference:			0.08		
	NHK	0.12	Cyto	0.230	6.43	0.52	0.2198	7.5%
			Default	0.414	6.95			
		0.25	Cyto	0.366	7.08	0.11	0.4073	1.5%
			Default	0.350	7.19			
		0.5	Cyto	0.331	7.86	-0.10	0.4073	-1.2%
			Default	0.220	7.76			
		1.25	Cyto	0.172	8.74	-0.03	0.5000	-0.3%
			Default	0.116	8.71			
		2	Cyto	0.095	9.18	-0.04	0.4073	-0.5%
			Default	0.062	9.14			
			Average Animal Difference:			0.09		
4	3T3	0.12	Cyto	0.100	6.53	0.81	**0.0485**	11.1%
			Default	0.381	7.35			
		0.25	Cyto	0.111	7.14	1.02	**0.0388**	12.5%
			Default	0.367	8.16			
		0.5	Cyto	0.072	7.68	1.20	**0.0152**	13.5%
			Default	0.376	8.88			
		1.25	Cyto	0.058	8.47	0.90	**0.0058**	9.6%
			Default	0.227	9.38			
		2	Cyto	0.066	8.90	0.66	**0.0058**	6.9%
			Default	0.151	9.56			
			Average Animal Difference:			0.92		
	NHK	0.12	Cyto	0.233	6.85	0.51	0.1627	7.0%
			Default	0.363	7.36			
		0.25	Cyto	0.182	7.35	0.84	**0.0603**	10.3%
			Default	0.322	8.20			
		0.5	Cyto	0.134	7.79	1.09	**0.0120**	12.3%
			Default	0.351	8.88			
		1.25	Cyto	0.083	8.56	0.85	**0.0074**	9.0%
			Default	0.209	9.42			
		2	Cyto	0.070	8.95	0.58	**0.0094**	6.0%
			Default	0.132	9.53			
			Average Animal Difference:			0.77		

Summary of Animals Used by GHS Toxicity Category and Cell Type

Toxcat	Cell	Sigma	Method	Std. Error	Animals	Difference	P-Value*	% Change
5	3T3	0.12	Cyto	0.313	7.01	2.17	**0.0018**	23.6%
			Default	0.247	9.17			
		0.25	Cyto	0.263	7.79	2.57	**0.0004**	24.8%
			Default	0.113	10.36			
		0.5	Cyto	0.189	8.33	2.49	**0.0004**	23.0%
			Default	0.071	10.82			
		1.25	Cyto	0.124	8.52	2.24	**0.0004**	20.8%
			Default	0.055	10.77			
		2	Cyto	0.097	8.61	1.85	**0.0004**	17.7%
			Default	0.049	10.45			
			Average Animal Difference:			2.26		
	NHK	0.12	Cyto	0.369	7.16	1.98	**0.0051**	21.7%
			Default	0.226	9.14			
		0.25	Cyto	0.296	7.92	2.42	**0.0004**	23.4%
			Default	0.093	10.34			
		0.5	Cyto	0.206	8.49	2.31	**0.0004**	21.4%
			Default	0.054	10.80			
		1.25	Cyto	0.117	8.68	2.06	**0.0004**	19.2%
			Default	0.047	10.74			
		2	Cyto	0.098	8.77	1.63	**0.0004**	15.7%
			Default	0.055	10.40			
			Average Animal Difference:			2.08		
6	3T3	0.12	Cyto	0.354	4.68	2.00	**0.0027**	30.0%
			Default	0.369	6.69			
		0.25	Cyto	0.427	5.87	2.04	**0.0086**	25.8%
			Default	0.433	7.91			
		0.5	Cyto	0.336	7.50	2.05	**0.0014**	21.5%
			Default	0.265	9.56			
		1.25	Cyto	0.250	8.43	2.47	**0.0007**	22.7%
			Default	0.058	10.90			
		2	Cyto	0.210	8.46	2.32	**0.0007**	21.5%
			Default	0.028	10.78			
			Average Animal Difference:			2.18		
	NHK	0.12	Cyto	0.362	4.94	1.70	**0.0068**	25.6%
			Default	0.344	6.64			
		0.25	Cyto	0.451	6.07	1.74	**0.0183**	22.3%
			Default	0.425	7.81			
		0.5	Cyto	0.353	7.71	1.79	**0.0021**	18.8%
			Default	0.274	9.49			
		1.25	Cyto	0.250	8.75	2.12	**0.0004**	19.5%
			Default	0.043	10.87			
		2	Cyto	0.244	8.78	2.04	**0.0004**	18.9%
			Default	0.027	10.82			
			Average Animal Difference:			1.88		

Notes:
*P-Value is from one-side Wilcoxon Signed Ranked test for difference in animal use between the default and cytotoxicity methods. **Boldfaced** values are significant values at $p < 0.05$.
Numbers are numbers of animals unless otherwise specified
Sigma - reciprocal of slope
Cyto= using NRU-predicted LD50 as starting dose
Default - using default starting dose of 175 mg/kg

Appendix Q-2

UDP Results for the RC Rat-Only Weight Regression – Starting at Estimated LD50 - 5000 mg/kg Upper

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UDP Results for the RC Rat-Only Weight Regression
Starting at Estimated LD50
5000 mg/kg Upper Limit
Results for 46 chemicals for the 3T3 NRU and 47 chemicals for the NHK NRU
(see notes to Table 6-5 for chemicals excluded)

Summary of Animals Used by Cell Type

Cell	Sigma	Method	Std. Error	Animals	Difference	P-Value*	% Savings
3T3	0.12	Cyto	0.305	7.03	1.11	**0.0033**	13.6%
		Default	0.250	8.15			
	0.25	Cyto	0.289	7.78	1.23	**0.0009**	13.7%
		Default	0.245	9.01			
	0.5	Cyto	0.239	8.52	1.28	**<.0001**	13.1%
		Default	0.206	9.80			
	1.25	Cyto	0.205	9.11	1.26	**<.0001**	12.2%
		Default	0.164	10.37			
	2	Cyto	0.180	9.27	1.05	**<.0001**	10.2%
		Default	0.131	10.32			
		Average Animal Difference:			1.19		
NHK	0.12	Cyto	0.331	7.08	1.06	**0.0036**	13.0%
		Default	0.247	8.14			
	0.25	Cyto	0.310	7.83	1.14	**0.0011**	12.7%
		Default	0.238	8.98			
	0.5	Cyto	0.256	8.59	1.20	**<.0001**	12.2%
		Default	0.198	9.79			
	1.25	Cyto	0.216	9.21	1.18	**<.0001**	11.4%
		Default	0.155	10.39			
	2	Cyto	0.193	9.35	0.99	**<.0001**	9.6%
		Default	0.123	10.34			
		Average Animal Difference:			1.12		

Summary of Animal Deaths by Cell Type

Cell Type	Sigma	Method	3 Animals at Limit Dose	5 Reversals	Likelihood Ratio	Max Animals	Animals Used	Animals Dead	% Deaths
3T3	0.12	Cyto	23.8%	50.7%	22.9%	2.6%	7.03	3.38	48.1%
		Default	23.3%	51.7%	21.5%	3.5%	8.15	3.45	42.4%
	0.25	Cyto	23.1%	30.7%	41.6%	4.6%	7.78	3.73	48.0%
		Default	22.5%	32.0%	38.0%	7.6%	9.01	3.81	42.3%
	0.5	Cyto	20.7%	18.4%	53.5%	7.4%	8.52	4.12	48.3%
		Default	19.6%	19.1%	47.7%	13.6%	9.80	4.19	42.8%
	1.25	Cyto	15.0%	12.7%	60.9%	11.3%	9.11	4.51	49.5%
		Default	13.3%	13.3%	53.0%	20.4%	10.37	4.64	44.7%
	2	Cyto	12.9%	11.9%	62.7%	12.6%	9.27	4.62	49.9%
		Default	10.5%	12.3%	56.6%	20.6%	10.32	4.74	45.9%
NHK	0.12	Cyto	25.4%	49.6%	21.7%	3.3%	7.08	3.34	47.2%
		Default	25.0%	50.9%	20.6%	3.5%	8.14	3.39	41.7%
	0.25	Cyto	24.5%	29.7%	40.5%	5.2%	7.83	3.69	47.2%
		Default	23.9%	31.6%	37.1%	7.4%	8.98	3.74	41.7%
	0.5	Cyto	21.9%	17.9%	52.3%	7.9%	8.59	4.09	47.6%
		Default	21.0%	18.9%	46.7%	13.4%	9.79	4.12	42.1%
	1.25	Cyto	15.6%	12.5%	59.9%	12.0%	9.21	4.51	49.0%
		Default	13.9%	13.2%	52.4%	20.5%	10.39	4.60	44.3%
	2	Cyto	12.7%	11.8%	62.2%	13.3%	9.35	4.63	49.5%
		Default	10.9%	12.4%	55.9%	20.9%	10.34	4.72	45.6%

Summary of Animals Used by GHS Toxicity Category and Cell Type

Toxcat	Cell	Sigma	Method	Std. Error	Animals	Difference	P-Value*	% Savings
1	3T3	0.12	Cyto	0.647	10.45	0.18	0.5000	1.6%
			Default	0.486	10.62			
		0.25	Cyto	0.637	11.06	0.19	0.4501	1.7%
			Default	0.330	11.24			
		0.5	Cyto	0.564	11.42	0.33	0.3538	2.8%
			Default	0.189	11.75			
		1.25	Cyto	0.513	11.70	0.34	0.4011	2.8%
			Default	0.126	12.04			
		2	Cyto	0.446	11.54	0.27	0.4254	2.3%
			Default	0.120	11.80			
			Average Animal Difference:			0.26		
	NHK	0.12	Cyto	0.541	11.36	-0.78	0.2670	-7.4%
			Default	0.531	10.58			
		0.25	Cyto	0.422	11.90	-0.85	0.0917	-7.7%
			Default	0.407	11.05			
		0.5	Cyto	0.355	12.19	-0.62	**0.0485**	-5.4%
			Default	0.264	11.57			
		1.25	Cyto	0.328	12.41	-0.45	**0.0485**	-3.8%
			Default	0.158	11.96			
		2	Cyto	0.335	12.16	-0.45	**0.0388**	-3.9%
			Default	0.131	11.70			
			Average Animal Difference:			-0.63		
2	3T3	0.12	Cyto	0.496	7.76	0.19	0.1618	2.4%
			Default	0.207	7.95			
		0.25	Cyto	0.574	8.59	-0.13	0.5000	-1.5%
			Default	0.105	8.46			
		0.5	Cyto	0.634	9.20	-0.21	0.5000	-2.4%
			Default	0.121	8.98			
		1.25	Cyto	0.595	9.65	-0.20	0.5000	-2.2%
			Default	0.110	9.45			
		2	Cyto	0.442	9.82	-0.23	0.5000	-2.4%
			Default	0.072	9.59			
			Average Animal Difference:			-0.12		
	NHK	0.12	Cyto	0.334	7.06	1.17	**0.0464**	14.2%
			Default	0.322	8.23			
		0.25	Cyto	0.268	7.84	0.87	0.0645	10.0%
			Default	0.187	8.72			
		0.5	Cyto	0.329	8.33	0.96	0.0645	10.3%
			Default	0.256	9.28			
		1.25	Cyto	0.266	8.82	0.92	**0.0464**	9.5%
			Default	0.220	9.74			
		2	Cyto	0.155	9.18	0.58	0.0645	5.9%
			Default	0.106	9.76			
			Average Animal Difference:			0.90		

Summary of Animals Used by GHS Toxicity Category and Cell Type

Toxcat	Cell	Sigma	Method	Std. Error	Animals	Difference	P-Value*	% Savings
3	3T3	0.12	Cyto	0.280	6.74	0.17	0.4688	2.5%
			Default	0.332	6.91			
		0.25	Cyto	0.238	7.23	-0.03	0.4688	-0.4%
			Default	0.258	7.21			
		0.5	Cyto	0.164	7.84	-0.04	0.5000	-0.5%
			Default	0.178	7.80			
		1.25	Cyto	0.101	8.74	-0.03	0.4688	-0.3%
			Default	0.087	8.72			
		2	Cyto	0.056	9.18	-0.06	0.1987	-0.7%
			Default	0.071	9.12			
			Average Animal Difference:			0.00		
	NHK	0.12	Cyto	0.214	6.52	0.52	0.2431	7.4%
			Default	0.377	7.04			
		0.25	Cyto	0.329	7.31	0.00	0.4073	0.0%
			Default	0.285	7.32			
		0.5	Cyto	0.309	8.02	-0.20	0.4688	-2.6%
			Default	0.196	7.82			
		1.25	Cyto	0.177	8.84	-0.14	0.2427	-1.6%
			Default	0.117	8.71			
		2	Cyto	0.107	9.19	-0.05	0.4688	-0.6%
			Default	0.068	9.13			
			Average Animal Difference:			0.03		
4	3T3	0.12	Cyto	0.246	6.80	0.54	0.1937	7.4%
			Default	0.382	7.34			
		0.25	Cyto	0.122	7.17	0.99	**0.0485**	12.1%
			Default	0.369	8.15			
		0.5	Cyto	0.045	7.60	1.28	**0.0094**	14.4%
			Default	0.375	8.88			
		1.25	Cyto	0.058	8.41	0.99	**0.0074**	10.5%
			Default	0.227	9.40			
		2	Cyto	0.056	8.89	0.67	**0.0045**	7.0%
			Default	0.155	9.56			
			Average Animal Difference:			0.89		
	NHK	0.12	Cyto	0.220	6.92	0.43	0.3089	5.9%
			Default	0.367	7.35			
		0.25	Cyto	0.132	7.27	0.89	0.0746	10.9%
			Default	0.336	8.16			
		0.5	Cyto	0.100	7.68	1.20	**0.0094**	13.5%
			Default	0.362	8.88			
		1.25	Cyto	0.079	8.53	0.87	**0.0074**	9.3%
			Default	0.215	9.40			
		2	Cyto	0.066	8.91	0.64	**0.0058**	6.7%
			Default	0.128	9.54			
			Average Animal Difference:			0.81		

Summary of Animals Used by GHS Toxicity Category and Cell Type

Toxcat	Cell	Sigma	Method	Std. Error	Animals	Difference	P-Value*	% Savings
5	3T3	0.12	Cyto	0.310	6.98	2.19	**0.0015**	23.9%
			Default	0.247	9.17			
		0.25	Cyto	0.278	7.73	2.64	**0.0004**	25.5%
			Default	0.112	10.37			
		0.5	Cyto	0.200	8.26	2.57	**0.0004**	23.7%
			Default	0.067	10.83			
		1.25	Cyto	0.115	8.49	2.28	**0.0004**	21.2%
			Default	0.056	10.78			
		2	Cyto	0.092	8.62	1.84	**0.0004**	17.6%
			Default	0.053	10.46			
			Average Animal Difference:			2.30		
	NHK	0.12	Cyto	0.370	7.08	2.07	**0.0044**	22.7%
			Default	0.227	9.15			
		0.25	Cyto	0.314	7.81	2.55	**0.0004**	24.6%
			Default	0.083	10.36			
		0.5	Cyto	0.215	8.36	2.47	**0.0004**	22.8%
			Default	0.047	10.83			
		1.25	Cyto	0.122	8.62	2.12	**0.0004**	19.7%
			Default	0.045	10.74			
		2	Cyto	0.103	8.71	1.70	**0.0004**	16.3%
			Default	0.049	10.41			
			Average Animal Difference:			2.18		
6	3T3	0.12	Cyto	0.393	4.68	2.00	**0.0045**	30.0%
			Default	0.369	6.69			
		0.25	Cyto	0.462	5.89	2.02	**0.0102**	25.5%
			Default	0.432	7.91			
		0.5	Cyto	0.330	7.48	2.07	**0.0014**	21.6%
			Default	0.262	9.55			
		1.25	Cyto	0.245	8.41	2.49	**0.0007**	22.8%
			Default	0.061	10.90			
		2	Cyto	0.204	8.44	2.33	**0.0007**	21.6%
			Default	0.032	10.77			
			Average Animal Difference:			2.18		
	NHK	0.12	Cyto	0.380	4.78	1.85	**0.0032**	27.9%
			Default	0.344	6.64			
		0.25	Cyto	0.463	5.90	1.91	**0.0105**	24.5%
			Default	0.426	7.81			
		0.5	Cyto	0.360	7.54	1.95	**0.0024**	20.6%
			Default	0.273	9.49			
		1.25	Cyto	0.250	8.56	2.33	**0.0004**	21.4%
			Default	0.045	10.89			
		2	Cyto	0.240	8.63	2.20	**0.0004**	20.3%
			Default	0.028	10.83			
			Average Animal Difference:			2.05		

*P-Value is from one-side Wilcoxon Signed Ranked test for difference in animal use between the default and cytotoxicity methods. **Boldfaced** values are significant values at $p < 0.05$.

Numbers are numbers of animals unless otherwise specified
Sigma - reciprocal of slope
Cyto= using NRU-predicted LD50 as starting dose
Default - using default starting dose of 175 mg/kg

Appendix Q-3

UDP Results for the RC Rat-Only Weight Regression Excluding Substances with Specific Mechanisms of Toxicity - Starting at Estimated LD50 – 5000 mg/kg Upper Limit

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UDP Results for the RC Rat-Only Weight Regression Excluding Substances with Specific Mechanisms of Toxicity Starting at Estimated LD50
5000 mg/kg Upper Limit
Results for 46 chemicals for the 3T3 NRU and 47 chemicals for the NHK NRU
(see notes to Table 6-5 for chemicals excluded)

Summary of Animals Used by Cell Type

Cell	Sigma	Method	Std. Error	Animals	Difference	P-Value*	% Savings
3T3	0.12	Cyto	0.328	7.10	1.07	0.0026	13.1%
		Default	0.243	8.18			
	0.25	Cyto	0.306	7.82	1.22	0.0011	13.5%
		Default	0.240	9.04			
	0.5	Cyto	0.256	8.57	1.24	<.0001	12.7%
		Default	0.204	9.82			
	1.25	Cyto	0.222	9.14	1.21	<.0001	11.7%
		Default	0.166	10.36			
	2	Cyto	0.199	9.28	1.05	<.0001	10.2%
		Default	0.131	10.33			
		Average Animal Difference:			1.16		

NHK	0.12	Cyto	0.334	7.08	1.07	0.0036	13.1%
		Default	0.245	8.15			
	0.25	Cyto	0.323	7.79	1.20	0.0007	13.4%
		Default	0.238	9.00			
	0.5	Cyto	0.273	8.54	1.26	<.0001	12.8%
		Default	0.200	9.80			
	1.25	Cyto	0.234	9.15	1.26	<.0001	12.1%
		Default	0.155	10.40			
	2	Cyto	0.212	9.30	1.04	<.0001	10.1%
		Default	0.123	10.34			
		Average Animal Difference:			1.17		

Summary of Animal Deaths by Cell Type

Cell Type	Sigma	Method	3 Animals at Limit Dose	5 Reversals	Likelihood Ratio	Max Animals	Animals Used	Animals Dead	% Deaths
3T3	0.12	Cyto	23.84%	49.81%	23.59%	2.76%	7.10	3.51	49.4%
		Default	23.33%	51.87%	21.28%	3.53%	8.18	3.47	42.4%
	0.25	Cyto	23.15%	30.80%	41.34%	4.71%	7.82	3.85	49.2%
		Default	22.47%	32.17%	37.75%	7.61%	9.04	3.83	42.3%
	0.5	Cyto	20.66%	18.46%	53.20%	7.68%	8.57	4.24	49.5%
		Default	19.61%	19.24%	47.50%	13.66%	9.82	4.20	42.8%
	1.25	Cyto	15.29%	12.83%	60.20%	11.68%	9.14	4.62	50.5%
		Default	13.30%	13.35%	53.00%	20.35%	10.36	4.63	44.8%
	2	Cyto	13.41%	11.68%	61.92%	13.00%	9.28	4.71	50.7%
		Default	10.49%	12.40%	56.43%	20.68%	10.33	4.75	45.9%
NHK	0.12	Cyto	25.41%	49.08%	22.59%	2.91%	7.08	3.45	48.7%
		Default	25.02%	50.91%	20.52%	3.55%	8.15	3.40	41.7%
	0.25	Cyto	24.68%	30.19%	39.88%	5.26%	7.79	3.79	48.6%
		Default	23.91%	31.89%	36.70%	7.50%	9.00	3.75	41.7%
	0.5	Cyto	22.22%	18.22%	51.54%	8.02%	8.54	4.18	48.9%
		Default	21.05%	18.94%	46.51%	13.50%	9.80	4.13	42.2%
	1.25	Cyto	16.09%	12.57%	59.43%	11.92%	9.15	4.58	50.1%
		Default	13.96%	13.21%	52.15%	20.68%	10.40	4.61	44.3%
	2	Cyto	13.56%	11.75%	61.29%	13.40%	9.30	4.69	50.4%
		Default	10.91%	12.40%	55.84%	20.84%	10.34	4.72	45.6%

Summary of Animals Used by GHS Toxicity Category and Cell Type

Toxcat	Cell	Sigma	Method	Std. Error	Animals	Difference	P-Value*	% Savings
1	3T3	0.12	Cyto	0.020	10.83	-0.33	0.3538	-3.1%
			Default	0.017	10.50			
		0.25	Cyto	0.022	11.35	-0.17	0.2670	-1.5%
			Default	0.019	11.18			
		0.5	Cyto	0.023	11.75	-0.05	0.1627	-0.4%
			Default	0.020	11.70			
		1.25	Cyto	0.025	11.96	0.05	0.3089	0.4%
			Default	0.023	12.01			
		2	Cyto	0.026	11.80	-0.01	0.2670	-0.1%
			Default	0.026	11.80			
			Average Animal Difference:			-0.10		
	NHK	0.12	Cyto	0.017	11.36	-0.83	0.2285	-7.9%
			Default	0.017	10.53			
		0.25	Cyto	0.019	12.08	-1.08	0.0603	-9.8%
			Default	0.019	11.00			
		0.5	Cyto	0.020	12.44	-0.90	**0.0193**	-7.8%
			Default	0.020	11.54			
		1.25	Cyto	0.022	12.65	-0.69	**0.0309**	-5.8%
			Default	0.024	11.96			
		2	Cyto	0.024	12.42	-0.73	**0.0245**	-6.2%
			Default	0.026	11.69			
			Average Animal Difference:			-0.85		
2	3T3	0.12	Cyto	0.019	8.39	-0.44	0.2732	-5.5%
			Default	0.015	7.95			
		0.25	Cyto	0.022	8.88	-0.46	0.3429	-5.5%
			Default	0.018	8.42			
		0.5	Cyto	0.026	9.44	-0.54	0.3429	-6.1%
			Default	0.023	8.90			
		1.25	Cyto	0.031	9.93	-0.61	0.3429	-6.5%
			Default	0.029	9.33			
		2	Cyto	0.032	10.00	-0.45	0.3429	-4.7%
			Default	0.030	9.55			
			Average Animal Difference:			-0.50		
	NHK	0.12	Cyto	0.017	7.53	0.67	0.0888	8.2%
			Default	0.016	8.20			
		0.25	Cyto	0.019	8.03	0.65	0.0645	7.5%
			Default	0.019	8.67			
		0.5	Cyto	0.023	8.39	0.82	0.0645	8.9%
			Default	0.024	9.21			
		1.25	Cyto	0.027	8.95	0.70	0.0645	7.3%
			Default	0.029	9.65			
		2	Cyto	0.030	9.32	0.42	0.0888	4.4%
			Default	0.031	9.74			
			Average Animal Difference:			0.65		

Summary of Animals Used by GHS Toxicity Category and Cell Type

Toxcat	Cell	Sigma	Method	Std. Error	Animals	Difference	P-Value*	% Savings
3	3T3	0.12	Cyto	0.013	7.11	0.11	0.3772	1.5%
			Default	0.015	7.23			
		0.25	Cyto	0.016	7.59	-0.21	0.1987	-2.8%
			Default	0.015	7.38			
		0.5	Cyto	0.020	8.16	-0.33	0.2431	-4.1%
			Default	0.018	7.84			
		1.25	Cyto	0.024	8.92	-0.28	0.1004	-3.2%
			Default	0.024	8.65			
		2	Cyto	0.026	9.28	-0.19	0.0782	-2.0%
			Default	0.026	9.10			
			Average Animal Difference:			-0.18		
	NHK	0.12	Cyto	0.014	7.11	0.00	0.5000	0.0%
			Default	0.014	7.10			
		0.25	Cyto	0.017	7.61	-0.31	0.4073	-4.2%
			Default	0.015	7.31			
		0.5	Cyto	0.021	8.24	-0.44	0.1987	-5.7%
			Default	0.018	7.79			
		1.25	Cyto	0.025	8.93	-0.22	0.3483	-2.5%
			Default	0.024	8.71			
		2	Cyto	0.027	9.30	-0.17	0.2431	-1.8%
			Default	0.026	9.13			
			Average Animal Difference:			-0.23		
4	3T3	0.12	Cyto	0.011	6.64	0.73	0.1118	9.9%
			Default	0.013	7.37			
		0.25	Cyto	0.014	7.21	1.01	**0.0485**	12.3%
			Default	0.017	8.23			
		0.5	Cyto	0.017	7.73	1.26	**0.0120**	14.0%
			Default	0.021	8.99			
		1.25	Cyto	0.021	8.44	0.99	**0.0074**	10.5%
			Default	0.025	9.43			
		2	Cyto	0.024	8.84	0.76	**0.0045**	7.9%
			Default	0.026	9.60			
			Average Animal Difference:			0.95		
	NHK	0.12	Cyto	0.013	7.00	0.38	0.2670	5.1%
			Default	0.013	7.38			
		0.25	Cyto	0.015	7.41	0.87	**0.0485**	10.5%
			Default	0.017	8.29			
		0.5	Cyto	0.017	7.84	1.11	**0.0152**	12.4%
			Default	0.021	8.95			
		1.25	Cyto	0.022	8.52	0.95	**0.0074**	10.0%
			Default	0.025	9.47			
		2	Cyto	0.023	8.84	0.70	**0.0058**	7.3%
			Default	0.026	9.54			
			Average Animal Difference:			0.80		

Summary of Animals Used by GHS Toxicity Category and Cell Type

Toxcat	Cell	Sigma	Method	Std. Error	Animals	Difference	P-Value*	% Savings
5	3T3	0.12	Cyto	0.012	6.77	2.42	**0.0004**	26.4%
			Default	0.014	9.20			
		0.25	Cyto	0.016	7.47	2.94	**0.0004**	28.2%
			Default	0.018	10.41			
		0.5	Cyto	0.018	8.02	2.86	**0.0004**	26.3%
			Default	0.020	10.88			
		1.25	Cyto	0.019	8.34	2.45	**0.0004**	22.7%
			Default	0.021	10.79			
		2	Cyto	0.019	8.50	1.98	**0.0004**	18.9%
			Default	0.022	10.48			
			Average Animal Difference:			2.53		
	NHK	0.12	Cyto	0.012	6.69	2.48	**0.0010**	27.1%
			Default	0.014	9.17			
		0.25	Cyto	0.016	7.38	3.05	**0.0004**	29.2%
			Default	0.018	10.43			
		0.5	Cyto	0.018	7.95	2.97	**0.0004**	27.2%
			Default	0.020	10.92			
		1.25	Cyto	0.019	8.32	2.48	**0.0004**	22.9%
			Default	0.021	10.80			
		2	Cyto	0.019	8.43	2.00	**0.0004**	19.2%
			Default	0.022	10.43			
			Average Animal Difference:			2.60		
6	3T3	0.12	Cyto	0.014	4.54	2.15	**0.0027**	32.1%
			Default	0.013	6.69			
		0.25	Cyto	0.020	5.76	2.15	**0.0102**	27.2%
			Default	0.020	7.91			
		0.5	Cyto	0.024	7.35	2.20	**0.0016**	23.0%
			Default	0.023	9.55			
		1.25	Cyto	0.024	8.28	2.63	**0.0007**	24.1%
			Default	0.023	10.91			
		2	Cyto	0.023	8.32	2.46	**0.0007**	22.8%
			Default	0.023	10.78			
			Average Animal Difference:			2.32		
	NHK	0.12	Cyto	0.013	4.58	2.05	**0.0032**	30.9%
			Default	0.012	6.64			
		0.25	Cyto	0.019	5.72	2.09	**0.0105**	26.8%
			Default	0.019	7.81			
		0.5	Cyto	0.023	7.34	2.15	**0.0015**	22.7%
			Default	0.022	9.49			
		1.25	Cyto	0.023	8.36	2.53	**0.0004**	23.2%
			Default	0.022	10.89			
		2	Cyto	0.022	8.46	2.38	**0.0004**	21.9%
			Default	0.022	10.84			
			Average Animal Difference:			2.24		

Notes:
*P-Value is from one-side Wilcoxon Signed Ranked test for difference in animal use between the default and cytotoxicity methods. **Boldfaced** values are significant values at $p < 0.05$.
Numbers are numbers of animals unless otherwise specified
Sigma - reciprocal of slope
Cyto= using NRU-predicted LD50 as starting dose
Default - using default starting dose of 175 mg/kg