Summary of Animals Used and Animals Dead for UDP Simulations by NRU Test Method[1]

NRU Test Method	Sigma	Starting Dose	Animals Used				Animals Died				% Savings - Animals Used	% Difference - Animals Died
			Std. Error	Number[2]	Difference[3]	P[4]	Std. Error	Number[2]	Difference[3]	P[4]		
3T3	0.12	Cyto	0.196	7.42	0.53	0.0002	0.204	3.43	0.00	0.6675	6.6%	0.1%
		Default	0.176	7.95			0.200	3.44				
	0.25	Cyto	0.189	8.15	0.52	0.0005	0.203	3.76	0.00	0.9311	6.0%	0.1%
		Default	0.178	8.68			0.197	3.76				
	0.50	Cyto	0.169	8.80	0.54	0.0008	0.191	4.09	0.02	0.6341	5.8%	0.5%
		Default	0.163	9.35			0.185	4.11				
	1.25	Cyto	0.135	9.34	0.61	0.0001	0.165	4.48	0.07	0.0238	6.1%	1.5%
		Default	0.131	9.95			0.152	4.55				
	2.00	Cyto	0.112	9.48	0.53	0.0003	0.145	4.60	0.07	0.0506	5.3%	1.5%
		Default	0.096	10.01			0.129	4.67				
			Average Difference		0.55		Average Difference		0.03			
NHK	0.12	Cyto	0.203	7.43	0.49	0.0003	0.215	3.39	-0.01	0.7372	6.2%	-0.2%
		Default	0.176	7.92			0.202	3.39				
	0.25	Cyto	0.197	8.18	0.48	0.0005	0.212	3.72	0.00	0.3125	5.6%	-0.1%
		Default	0.174	8.66			0.198	3.72				
	0.50	Cyto	0.176	8.86	0.50	0.0006	0.199	4.07	0.01	0.2841	5.3%	0.2%
		Default	0.157	9.36			0.183	4.08				
	1.25	Cyto	0.145	9.41	0.55	0.0002	0.173	4.48	0.04	0.0129	5.5%	1.0%
		Default	0.125	9.96			0.150	4.52				
	2.00	Cyto	0.121	9.53	0.49	0.0001	0.151	4.61	0.05	0.0206	4.9%	1.1%
		Default	0.092	10.01			0.127	4.66				
			Average Difference		0.50		Average Difference		0.02			

Abbreviations: UDP=Up-and-Down Procedure (OECD 2001a, EPA 2002a); NRU=Neutral red uptake; Sigma=Reciprocal of dose-mortality slope; Cyto=NRU-determined starting dose (i.e., one dose lower than the LD_{50} predicted by the NRU IC_{50} in the RC rat-only millimole regression (log LD_{50} [mmol/kg] = 0.439 log IC_{50} [mM] + 0.621); Default=Default starting dose of 175 mg/kg; Std. Error=Standard error for number of animals; 3T3= BALB/c 3T3 mouse fibroblasts; NHK=Normal human epidermal keratinocytes; RC=Registry of Cytotoxicity..

[1]For 10,000 UDP simulations at each starting dose and dose-mortality slope for 67 substances in the 3T3 NRU test method and 68 substances in the NHK NRU test method. Upper limit dose =5000 mg/kg.

[2]Mean number of animals for 10,000 simulations.

[3]Difference between mean number of animals for the default starting dose and mean number of animals for the NRU-based starting dose.

[4]P-value is from one-sided Wilcoxon signed rank test for difference in animals between the default and NRU-based starting doses. Significant values at $p < 0.05$.

Summary of Stopping Rules Used for the UDP Simulations by NRU Test Method[1]

NRU Test Method	Sigma	Starting Dose	3 Animals at Limit Dose[2]	5 Reversals[2]	Likelihood Ratio[2]	Maximum Number of Animals Used[2]
3T3	0.12	Cyto	15.6%	56.0%	26.4%	2.0%
		Default	15.4%	56.9%	25.3%	2.4%
	0.25	Cyto	15.0%	33.6%	47.4%	4.0%
		Default	14.7%	34.1%	46.0%	5.3%
	0.5	Cyto	13.4%	19.8%	59.0%	7.8%
		Default	13.0%	20.0%	57.3%	9.7%
	1.25	Cyto	9.8%	13.5%	64.0%	12.7%
		Default	9.1%	13.6%	60.9%	16.4%
	2	Cyto	8.5%	12.3%	65.2%	14.0%
		Default	7.4%	12.5%	62.6%	17.5%
NHK	0.12	Cyto	16.8%	55.3%	26.0%	1.8%
		Default	16.6%	56.0%	25.0%	2.4%
	0.25	Cyto	16.1%	33.3%	46.5%	4.1%
		Default	15.8%	33.5%	45.5%	5.2%
	0.5	Cyto	14.3%	19.7%	58.0%	8.1%
		Default	13.8%	19.9%	56.6%	9.7%
	1.25	Cyto	10.1%	13.5%	63.1%	13.3%
		Default	9.5%	13.5%	60.4%	16.5%
	2	Cyto	8.6%	12.3%	64.6%	14.5%
		Default	7.6%	12.5%	62.3%	17.6%

Abbreviations: UDP=Up-and-Down Procedure (OECD 2001a, EPA 2002a); NRU=Neutral red uptake; Sigma=Reciprocal of dose-mortality slope; Cyto=NRU-determined starting dose (i.e., one dose lower than the LD_{50} predicted by the NRU IC_{50} in the RC rat-only millimole regression (log LD_{50} [mmol/kg] = 0.439 log IC_{50} [mM] + 0.621); Default=Default starting dose of 175 mg/kg; 3T3= BALB/c 3T3 mouse fibroblasts; NHK=Normal human epidermal keratinocytes; RC=Registry of Cytotoxicity.

[1]For 10,000 UDP simulations at each starting dose and dose-mortality slope for 67 substances in the 3T3 NRU test method and 68 substances in the NHK NRU test method. Upper limit dose =5000 mg/kg.

[2]Percentage of the 10,000 test simulations that satisfied the specified condition for completion of testing (see OECD [2001a]; EPA [2002a]).

Summary of Animals Used and Animals Dead for UDP Simulations by GHS Toxicity Category and NRU Test Method[1]

Toxcat	NRU Test Method	Sigma	Starting Dose	Animals Used				Animals Died				% Savings - Animals Used	% Difference - Animals Died
				Std. Error	Number[2]	Difference[3]	P[4]	Std. Error	Number[2]	Difference[3]	P[4]		
1	3T3	0.12	Cyto	0.431	8.74	0.96	0.6250	0.459	5.58	0.81	0.6250	9.9%	12.7%
			Default	0.277	9.70			0.170	6.39				
		0.25	Cyto	0.660	9.56	1.02	0.6250	0.581	6.06	0.84	0.6250	9.7%	12.2%
			Default	0.179	10.58			0.155	6.90				
		0.50	Cyto	0.697	10.19	1.14	0.6250	0.609	6.46	0.91	0.6250	10.0%	12.3%
			Default	0.201	11.32			0.197	7.37				
		1.25	Cyto	0.664	10.68	1.07	0.6250	0.598	6.70	0.87	0.6250	9.1%	11.5%
			Default	0.156	11.75			0.169	7.57				
		2.00	Cyto	0.548	10.65	0.82	0.6250	0.506	6.54	0.71	0.6250	7.1%	9.8%
			Default	0.146	11.47			0.152	7.24				
				Average Difference		1.00		Average Difference		0.83			
	NHK	0.12	Cyto	0.516	8.95	0.71	0.3750	0.531	5.79	0.58	0.3750	7.3%	9.1%
			Default	0.268	9.66			0.169	6.37				
		0.25	Cyto	0.699	9.77	0.77	0.3750	0.626	6.26	0.61	0.3750	7.3%	8.9%
			Default	0.217	10.53			0.177	6.87				
		0.50	Cyto	0.707	10.47	0.75	0.3750	0.638	6.69	0.63	0.3750	6.7%	8.6%
			Default	0.241	11.21			0.224	7.31				
		1.25	Cyto	0.692	10.92	0.78	0.3750	0.636	6.91	0.65	0.3750	6.7%	8.6%
			Default	0.169	11.70			0.179	7.56				
		2.00	Cyto	0.627	10.81	0.66	0.3750	0.578	6.70	0.53	0.3750	5.7%	7.4%
			Default	0.159	11.47			0.157	7.24				
				Average Difference		0.73		Average Difference		0.60			
2	3T3	0.12	Cyto	0.467	8.54	-0.08	0.8926	0.426	5.16	-0.05	0.9460	-1.0%	-1.0%
			Default	0.278	8.46			0.239	5.11				
		0.25	Cyto	0.426	9.21	-0.13	0.8926	0.404	5.54	-0.07	0.9460	-1.4%	-1.3%
			Default	0.210	9.08			0.202	5.47				
		0.50	Cyto	0.453	9.74	-0.07	1.0000	0.417	5.83	-0.06	1.0000	-0.7%	-1.0%
			Default	0.230	9.68			0.211	5.77				
		1.25	Cyto	0.413	10.25	-0.08	0.9460	0.394	6.06	-0.09	0.8926	-0.8%	-1.5%
			Default	0.236	10.17			0.218	5.97				
		2.00	Cyto	0.328	10.34	-0.14	0.5879	0.335	6.01	-0.10	0.7354	-1.4%	-1.8%
			Default	0.177	10.20			0.178	5.91				
				Average Difference		-0.10		Average Difference		-0.07			
	NHK	0.12	Cyto	0.488	8.77	-0.33	0.3757	0.476	5.26	-0.15	0.5879	-3.9%	-3.0%
			Default	0.260	8.43			0.232	5.11				
		0.25	Cyto	0.428	9.44	-0.36	0.4143	0.444	5.64	-0.17	0.6848	-4.0%	-3.1%
			Default	0.166	9.08			0.187	5.46				
		0.50	Cyto	0.448	9.99	-0.34	0.3757	0.453	5.94	-0.18	0.5417	-3.5%	-3.2%
			Default	0.164	9.65			0.185	5.75				
		1.25	Cyto	0.424	10.46	-0.32	0.3396	0.440	6.16	-0.21	0.4973	-3.2%	-3.5%
			Default	0.183	10.14			0.196	5.95				
		2.00	Cyto	0.348	10.49	-0.32	0.4143	0.381	6.09	-0.20	0.5417	-3.1%	-3.4%
			Default	0.148	10.18			0.166	5.89				
				Average Difference		-0.33		Average Difference		-0.18			

Summary of Animals Used and Animals Dead for UDP Simulations by GHS Toxicity Category and NRU Test Method[1]

Toxcat	NRU Test Method	Sigma	Starting Dose	Animals Used				Animals Died				% Savings - Animals Used	% Difference - Animals Died
				Std. Error	Number[2]	Difference[3]	P[4]	Std. Error	Number[2]	Difference[3]	P[4]		
3	3T3	0.12	Cyto	0.189	6.90	-0.29	0.0425	0.149	3.60	-0.23	0.0522	-4.3%	-6.8%
			Default	0.188	6.61			0.125	3.37				
		0.25	Cyto	0.220	7.53	-0.33	0.0522	0.169	3.96	-0.24	0.0640	-4.6%	-6.6%
			Default	0.152	7.20			0.103	3.71				
		0.50	Cyto	0.213	8.18	-0.42	0.0522	0.163	4.31	-0.27	0.0640	-5.5%	-6.7%
			Default	0.101	7.76			0.080	4.04				
		1.25	Cyto	0.141	8.98	-0.35	0.0522	0.123	4.69	-0.22	0.0771	-4.1%	-4.9%
			Default	0.059	8.62			0.057	4.47				
		2.00	Cyto	0.084	9.33	-0.23	0.0522	0.094	4.85	-0.15	0.2036	-2.5%	-3.3%
			Default	0.040	9.10			0.050	4.70				
				Average Difference		-0.33		Average Difference		-0.22			
	NHK	0.12	Cyto	0.190	6.85	-0.28	0.1514	0.133	3.52	-0.16	0.2334	-4.2%	-4.9%
			Default	0.190	6.57			0.127	3.35				
		0.25	Cyto	0.229	7.48	-0.31	0.0425	0.152	3.86	-0.17	0.1099	-4.4%	-4.6%
			Default	0.159	7.17			0.106	3.69				
		0.50	Cyto	0.206	8.12	-0.34	0.0923	0.143	4.20	-0.16	0.2036	-4.4%	-4.1%
			Default	0.109	7.78			0.082	4.04				
		1.25	Cyto	0.120	8.93	-0.28	0.0522	0.108	4.60	-0.12	0.4697	-3.2%	-2.6%
			Default	0.061	8.65			0.060	4.48				
		2.00	Cyto	0.079	9.31	-0.20	0.0923	0.088	4.77	-0.07	0.7334	-2.2%	-1.5%
			Default	0.036	9.11			0.048	4.70				
				Average Difference		-0.28		Average Difference		-0.14			
4	3T3	0.12	Cyto	0.191	7.15	0.31	0.0443	0.063	3.39	0.01	0.9399	4.1%	0.2%
			Default	0.235	7.46			0.066	3.40				
		0.25	Cyto	0.186	7.66	0.28	0.0507	0.032	3.61	-0.003	0.2522	3.5%	-0.1%
			Default	0.201	7.94			0.048	3.60				
		0.50	Cyto	0.210	8.14	0.38	0.1046	0.040	3.80	0.05	0.1591	4.5%	1.4%
			Default	0.212	8.53			0.049	3.86				
		1.25	Cyto	0.180	8.82	0.33	0.0250	0.049	4.10	0.03	0.0934	3.6%	0.8%
			Default	0.145	9.16			0.022	4.13				
		2.00	Cyto	0.133	9.16	0.22	0.0577	0.042	4.26	-0.01	0.8603	2.3%	-0.2%
			Default	0.084	9.38			0.019	4.25				
				Average Difference		0.31		Average Difference		0.02			
	NHK	0.12	Cyto	0.196	7.00	0.49	0.0073	0.064	3.36	0.06	0.1439	6.5%	1.7%
			Default	0.247	7.49			0.071	3.42				
		0.25	Cyto	0.213	7.53	0.45	0.0131	0.036	3.58	0.05	0.0577	5.6%	1.4%
			Default	0.207	7.97			0.048	3.63				
		0.50	Cyto	0.234	8.03	0.52	0.0335	0.041	3.78	0.09	0.0654	6.1%	2.4%
			Default	0.221	8.55			0.052	3.88				
		1.25	Cyto	0.218	8.76	0.41	0.0182	0.051	4.10	0.04	0.1297	4.5%	1.1%
			Default	0.147	9.17			0.023	4.14				
		2.00	Cyto	0.163	9.12	0.27	0.0443	0.042	4.28	-0.02	0.8999	2.9%	-0.4%
			Default	0.086	9.40			0.018	4.26				
				Average Difference		0.43		Average Difference		0.05			

Summary of Animals Used and Animals Dead for UDP Simulations by GHS Toxicity Category and NRU Test Method[1]

Toxcat	NRU Test Method	Sigma	Starting Dose	Animals Used				Animals Died				% Savings - Animals Used	% Difference - Animals Died
				Std. Error	Number[2]	Difference[3]	P[4]	Std. Error	Number[2]	Difference[3]	P[4]		
5	3T3	0.12	Cyto	0.308	7.96	1.21	0.0020	0.042	3.25	0.06	0.0137	13.2%	1.7%
			Default	0.232	9.17			0.034	3.30				
		0.25	Cyto	0.196	9.01	1.33	0.0039	0.049	3.46	0.11	0.0195	12.8%	3.1%
			Default	0.157	10.34			0.062	3.57				
		0.50	Cyto	0.148	9.46	1.28	0.0039	0.051	3.56	0.09	0.0195	11.9%	2.5%
			Default	0.102	10.73			0.059	3.65				
		1.25	Cyto	0.131	9.29	1.38	0.0020	0.038	3.67	0.20	0.0020	12.9%	5.2%
			Default	0.065	10.66			0.030	3.87				
		2.00	Cyto	0.107	9.20	1.16	0.0039	0.032	3.78	0.18	0.0039	11.2%	4.6%
			Default	0.061	10.36			0.013	3.96				
				Average Difference		1.27		Average Difference		0.13			
	NHK	0.12	Cyto	0.285	8.06	1.11	0.0020	0.030	3.25	0.06	0.0273	12.1%	1.7%
			Default	0.233	9.17			0.038	3.31				
		0.25	Cyto	0.241	9.12	1.19	0.0020	0.048	3.47	0.10	0.0273	11.5%	2.8%
			Default	0.152	10.31			0.061	3.56				
		0.50	Cyto	0.200	9.54	1.21	0.0020	0.046	3.55	0.10	0.0098	11.3%	2.7%
			Default	0.082	10.75			0.064	3.65				
		1.25	Cyto	0.167	9.40	1.27	0.0039	0.030	3.68	0.18	0.0039	11.9%	4.7%
			Default	0.052	10.66			0.037	3.86				
		2.00	Cyto	0.131	9.28	1.06	0.0020	0.029	3.79	0.17	0.0020	10.3%	4.2%
			Default	0.037	10.35			0.022	3.96				
				Average Difference		1.17		Average Difference		0.12			
6	3T3	0.12	Cyto	0.685	6.18	1.58	0.0005	0.314	0.88	-0.02	0.0923	20.3%	-2.8%
			Default	0.587	7.76			0.304	0.85				
		0.25	Cyto	0.647	7.10	1.57	0.0005	0.316	1.33	-0.03	0.0342	18.1%	-2.1%
			Default	0.541	8.67			0.309	1.30				
		0.50	Cyto	0.486	8.29	1.58	0.0005	0.255	2.04	-0.01	0.1294	16.0%	-0.4%
			Default	0.342	9.87			0.255	2.03				
		1.25	Cyto	0.301	9.01	1.88	0.0005	0.126	3.00	0.19	0.0005	17.3%	6.0%
			Default	0.058	10.89			0.121	3.19				
		2.00	Cyto	0.246	8.94	1.81	0.0005	0.088	3.33	0.28	0.0005	16.8%	7.7%
			Default	0.030	10.75			0.066	3.60				
				Average Difference		1.68		Average Difference		0.08			
	NHK	0.12	Cyto	0.630	6.19	1.47	0.0002	0.298	0.82	-0.02	0.0281	19.2%	-3.1%
			Default	0.560	7.66			0.289	0.80				
		0.25	Cyto	0.585	7.16	1.47	0.0002	0.295	1.28	-0.02	0.1099	17.0%	-1.7%
			Default	0.499	8.63			0.287	1.26				
		0.50	Cyto	0.440	8.41	1.47	0.0002	0.236	2.03	-0.01	0.0942	14.8%	-0.7%
			Default	0.317	9.87			0.236	2.02				
		1.25	Cyto	0.276	9.14	1.73	0.0002	0.112	3.02	0.16	0.0002	16.0%	5.0%
			Default	0.056	10.87			0.114	3.18				
		2.00	Cyto	0.234	9.06	1.69	0.0002	0.078	3.36	0.25	0.0002	15.7%	7.0%
			Default	0.022	10.74			0.062	3.61				
				Average Difference		1.56		Average Difference		0.07			

Abbreviations: UDP=Up-and-Down Procedure (OECD 2001a, EPA 2002a); Toxcat=Category from Globally Harmonized System of Classification and Labeling of Chemicals[5] (GHS; UN 2005); NRU=Neutral red uptake; Sigma=Reciprocal of dose-mortality slope; Cyto=NRU-determined starting dose (i.e., one dose lower than the LD_{50} predicted by the NRU IC_{50} in the RC rat-only millimole regression (log LD_{50} [mmol/kg] = 0.439 log IC_{50} [mM] + 0.621); Default=Default starting dose of 175 mg/kg; Std. Error=Standard error for number of animals; 3T3= BALB/c 3T3 mouse fibroblasts; NHK=Normal human epidermal keratinocytes; RC=Registry of Cytotoxicity.

[1]For 10,000 UDP simulations at each starting dose and dose-mortality slope for 67 substances in the 3T3 NRU test method and 68 substances in the NHK NRU test method. Upper limit dose =5000 mg/kg.

[1]For 10,000 UDP simulations at each starting dose and dose-mortality slope for 67 substances in the 3T3 NRU test method and 68 substances in the NHK NRU test method. Upper limit dose =5000 mg/kg.

[2]Mean number of animals for 10,000 simulations.

[3]Difference between mean animals used for the default starting dose and mean animals used for the NRU-based starting dose.

[4]P-value is from one-side Wilcoxon signed rank test for difference in animals between the default and NRU-based starting doses. Significant values at $p < 0.05$.

[5]GHS Toxicity Category	Oral LD_{50} Limits
1	$LD_{50} \leq 5$ mg/kg
2	$5 < LD_{50} \leq 50$ mg/kg
3	$50 < LD_{50} \leq 300$ mg/kg
4	$300 < LD_{50} \leq 2000$ mg/kg
5	$2000 < LD_{50} \leq 5000$ mg/kg
6	$LD_{50} > 5000$ mg/kg

Concordance of NRU-Based Starting Dose with Default Starting Dose for GHS Acute Oral Toxicity Category Outcome Based on Simulated UDP LD_{50}[1]

GHS Category Based on LD_{50} Outcome with Default Starting Dose	GHS Category[2] Based on LD_{50} Outcome with NHK NRU-Based Starting Dose									
	1	2	3	4	5	6	Total	Category Match	Higher NRU Category	Lower NRU Category
1	4	0	0	0	0	0	4	100%	0%	0%
2	0	13	0	0	0	0	13	100%	0%	0%
3	0	1	11	0	0	0	12	92%	0%	8%
4	0	0	1	15	1	0	17	88%	6%	6%
5	0	0	0	0	22	0	22	100%	0%	0%
6	0	0	0	0	0	0	0	NA	0%	NA
Total	4	14	12	15	23	0	68	96%	1%	3%

GHS Category Based on LD_{50} Outcome with Default Starting Dose	GHS Category[2] Based on LD_{50} Outcome with 3T3 NRU-Based Starting Dose									
	1	2	3	4	5	6	Total	Category Match	Higher NRU Category	Lower NRU Category
1	4	0	0	0	0	0	4	100%	0%	0%
2	0	13	0	0	0	0	13	100%	0%	0%
3	0	1	11	0	0	0	12	92%	0%	8%
4	0	0	0	16	1	0	17	94%	6%	0%
5	0	0	0	0	21	0	21	100%	0%	0%
6	0	0	0	0	0	0	0	NA	0%	NA
Total	4	14	11	16	22	0	67	97%	1%	1%

Abbreviations: NRU=Neutral red uptake; GHS=Globally Harmonized System of Classification and Labelling of Chemicals (UN 2005); UDP=Up-and-Down Procedure (OECD 2001a, EPA 2002a); NHK=Normal human epidermal keratinocytes; 3T3= BALB/c 3T3 mouse fibroblasts; NA=Not applicable; RC=Registry of Cytotoxicity.

[1]For 10,000 UDP simulations at each starting dose and dose-mortality slope for 67 substances in the 3T3 NRU test method and 68 substances in the NHK NRU test method. Upper limit dose =5000 mg/kg. The NRU-based starting dose was one dose lower than the LD_{50} predicted by the NRU IC_{50} in the RC rat-only millimole regression (log LD_{50} [mmol/kg] = 0.439 log IC_{50} [mM] + 0.621). The default starting dose = 175 mg/kg. Shaded cells are those containing the correct predictions.

[2]GHS Toxicity Category	Oral LD_{50} Limits
1	$LD_{50} \leq 5$ mg/kg
2	$5 < LD_{50} \leq 50$ mg/kg
3	$50 < LD_{50} \leq 300$ mg/kg
4	$300 < LD_{50} \leq 2000$ mg/kg
5	$2000 < LD_{50} \leq 5000$ mg/kg
6	$LD_{50} > 5000$ mg/kg

Discordant Substances for GHS Category Outcomes of UDP Simulations[1]

NRU Test Method	Substance	NRU-Based Starting Dose[2]		Default Starting Dose[3]		LD_{50} Difference
		LD_{50}	Toxcat[4]	LD_{50}	Toxcat[4]	
3T3	Acetaminophen	2046.78	5	1765.44	4	-281.34
	Sodium Dichromate Dihydrate	43.70	2	51.87	3	8.17
NHK	Acetaminophen	2173.95	5	1755.26	4	-418.69
	Caffeine	279.63	3	357.17	4	77.55
	Sodium Dichromate Dihydrate	45.09	2	51.77	3	6.69

Abbreviations: Toxcat=Globally Harmonized System of Classification and Labelling of Chemicals (GHS; UN 2005); UDP= Up-and-Down Procedure (OECD 2001a, EPA 2002a); NRU=Neutral red uptake; 3T3=BALB/c 3T3 mouse fibroblasts; NHK=Normal human epidermal keratinocytes.

[1]Substances for which the simulated UDP outcome (in terms of GHS category) at the NRU-based starting dose did not match the simulated UDP outcome at the default starting dose. Simulations were performed with 10,000 runs at each starting dose and dose-mortality slope for 67 substances in the 3T3 NRU test method and 68 substances in the NHK NRU test method. Upper limit dose =5000 mg/kg.

[2]NRU-based starting dose was one dose lower than the LD_{50} predicted by the NRU IC_{50} in the RC rat-only millimole regression (log LD_{50} [mmol/kg] = 0.439 log IC_{50} [mM] + 0.621).

[3]The default starting dose = 175 mg/kg. Shaded cells are those containing the correct predictions.

[4]

GHS Toxicity Category	Oral LD_{50} Limits
1	$LD_{50} \leq 5$ mg/kg
2	$5 < LD_{50} \leq 50$ mg/kg
3	$50 < LD_{50} \leq 300$ mg/kg
4	$300 < LD_{50} \leq 2000$ mg/kg
5	$2000 < LD_{50} \leq 5000$ mg/kg
6	$LD_{50} > 5000$ mg/kg