

## Appendix J

### LD<sub>50</sub> and Toxicity Category Predictions

<b>J-1</b>	<b>3T3 NRU Predictions: RC Millimole Regression .....</b>	<b>J-7</b>
<b>J-2</b>	<b>3T3 NRU Predictions: 3T3 Combined-Laboratory Regression .....</b>	<b>J-11</b>
<b>J-3</b>	<b>NHK NRU Predictions: RC Millimole Regression .....</b>	<b>J-17</b>
<b>J-4</b>	<b>NHK NRU Predictions: NHK Combined-Laboratory Regression .....</b>	<b>J-21</b>
<b>J-5</b>	<b>3T3 NRU Predictions: RC Rat-Only Weight Regression .....</b>	<b>J-27</b>
<b>J-6</b>	<b>NHK NRU Predictions: RC Rat-Only Weight Regression .....</b>	<b>J-31</b>
<b>J-7</b>	<b>3T3 NRU Predictions: RC Rat-Only Weight Regression Excluding Chemicals with Specific Mechanisms of Toxicity ....</b>	<b>J-35</b>
<b>J-8</b>	<b>NHK NRU Predictions: RC Rat-Only Weight Regression Excluding Chemicals with Specific Mechanisms of Toxicity ....</b>	<b>J-39</b>

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## Appendix J

Data for the same reference chemicals were evaluated for each regression in **Appendices J-1, J-3, J-5, J-6, J-7, and J-8**. Forty-six chemicals were evaluated for the 3T3 NRU test method and 47 chemicals were evaluated for the NHK NRU test method. Of the original 72 chemicals tested, epinephrine bitartrate, colchicine, and propylparaben were excluded because they were removed from the calculation of the RC rat-only weight regression due to the lack of rat oral reference LD<sub>50</sub> data. The 21 chemicals with specific mechanisms of toxicity in **Table 6-3** were excluded from all analyses to be consistent with those removed from the RC rat-only weight regression. These chemicals have known mechanisms of toxicity that are not expected to be active in the 3T3 and NHK cell cultures. Carbon tetrachloride and methanol were excluded from the 3T3 NRU evaluations because no laboratory attained sufficient toxicity in any experiment for the calculation of an IC<sub>50</sub>. Carbon tetrachloride was also excluded from the NHK NRU evaluations because no laboratory attained sufficient toxicity in any experiment for the calculation of an IC<sub>50</sub>.

**Appendix J-2**, which contains the data for the 3T3 combined-laboratory regression, uses 70 chemicals and **Appendix J-4**, which contains the data for the NHK combined-laboratory regression, uses 71 chemicals. No laboratory achieved sufficient toxicity for calculation of an IC<sub>50</sub> for carbon tetrachloride or methanol with the 3T3 NRU test method or for carbon tetrachloride with the NHK NRU test method.

### **RC Millimole Regression: Appendices J-1 (3T3 NRU) and J-3 (NHK NRU)**

$$\text{Log } LD_{50} \text{ (mmol/kg)} = 0.435 \text{ log } IC_{50} \text{ (mM)} + 0.625$$

Predicted LD<sub>50</sub> values in mmol/kg and mg/kg (conversion from the mmol/kg values) were determined for each cell type using the respective IC<sub>50</sub> values in the RC equation. The predicted log LD<sub>50</sub> value was subtracted from the observed log (RC original) LD<sub>50</sub> value and the difference (positive or negative) was compared to the RC criterion for outliers (0.699). Reference substances with absolute values greater than 0.699 were identified as positive or negative outliers to the RC millimole regression. The observed (RC original) LD<sub>50</sub> value (mg/kg) was used to assign each reference chemical to an observed toxicity category (GHS classification). The

predicted LD<sub>50</sub> value (mg/kg) was used determine the reference substance's predicted toxicity category.

#### **Combined-Laboratory Regressions: Appendices J-2 (3T3 NRU) and J-4 (NHK NRU)**

**3T3**       $\text{Log } LD_{50} (\text{mmol/kg}) = 0.589 \text{ log } IC_{50} (\text{mM}) + 0.425$

**NHK**       $\text{Log } LD_{50} (\text{mmol/kg}) = 0.510 \text{ log } IC_{50} (\text{mM}) + 0.452$

Regressions were determined using the respective geometric mean IC<sub>50</sub> values (mM) and the NICEATM reference LD<sub>50</sub> values (mmol/kg) from **Table 4-2**. Predicted LD<sub>50</sub> values in mmol/kg and mg/kg (conversion from the mmol/kg values) were then determined using the IC<sub>50</sub> values in the equation. The predicted log LD<sub>50</sub> value was subtracted from the observed (NICEATM reference) log LD<sub>50</sub> value and the difference (positive or negative) was compared to the respective statistical value for outliers using the 90% prediction interval (1.510 – 1.573 for the 3T3 NRU and 1.639 – 1.701 for the NHK NRU). Reference substances with absolute values greater than the prediction value were identified as positive or negative statistical outliers to the respective regression. The observed (reference) LD<sub>50</sub> value (mg/kg) was used to assign each reference substance to an observed toxicity category (GHS classification). The predicted LD<sub>50</sub> value (mg/kg) was used to assign the reference substance's predicted toxicity category.

Regressions are based on a single point per chemical (i.e., the geometric mean of the geometric mean IC<sub>50</sub> values obtained for each laboratory and the NICEATM reference rodent oral LD<sub>50</sub> from **Table 4-2**). The 3T3 combined-laboratory regression uses the data for 70 chemicals and the NHK combined-laboratory regression uses the data for 71 chemicals. No laboratory achieved sufficient toxicity for calculation of an IC<sub>50</sub> for carbon tetrachloride or methanol with the 3T3 NRU test method or for carbon tetrachloride with the NHK NRU test method.

#### **RC Rat-Only Weight Regression: Appendices J-5 (3T3 NRU) and J-6 (NHK NRU)**

$\text{Log } LD_{50} \text{ mg/kg} = 0.372 \text{ log } IC_{50} \mu\text{g/mL} + 2.024$

The regression was determined by using the RC IC<sub>50</sub> and LD<sub>50</sub> data for the 282 chemicals that had rat oral LD<sub>50</sub> values. The regression data were converted into weight units (i.e., LD<sub>50</sub> values as mg/kg and IC<sub>50</sub> values as µg/mL). Predicted LD<sub>50</sub> values for the 3T3 NRU (**Appendix J-5**) and the NHK NRU (**Appendix J-6**) were determined using the geometric mean of the geometric

mean IC<sub>50</sub> values obtained for each laboratory in the regression equation. The observed (NICEATM reference) LD<sub>50</sub> value (mg/kg) from **Table 4-2** was used to assign each reference substance to an observed toxicity category (GHS classification). The predicted LD<sub>50</sub> value (mg/kg) was used to determine the reference substance's predicted toxicity category.

**RC Rat-Only Weight Regression Excluding Chemicals with Specific Mechanisms of Toxicity: Appendices J-7 (3T3 NRU) and J-8 (NHK NRU)**

$$\text{Log } LD_{50} \text{ mg/kg} = 0.357 \text{ log } IC_{50} \text{ } \mu\text{g/mL} + 2.194$$

This regression was determined by excluding the 50 chemicals with specific mechanisms of action that are not expected to be active in the 3T3 and NHK cell cultures (i.e., likely to confer outlier status for an individual chemical) from the 282 RC chemicals that had rat LD<sub>50</sub> values (see **Section 6.2.3** and **Appendix K-3**). The regression data were converted into weight units (i.e., LD<sub>50</sub> values as mg/kg and IC<sub>50</sub> values as  $\mu\text{g/mL}$ ). Predicted LD<sub>50</sub> values for the 3T3 NRU (**Appendix J-7**) and the NHK NRU (**Appendix J-8**) were determined using the geometric mean IC<sub>50</sub> values (of the geometric means generated by the three laboratories in the study) in the regression. The observed (NICEATM reference) LD<sub>50</sub> value (mg/kg) was used to assign each reference substance to an observed toxicity category (GHS classification). The predicted LD<sub>50</sub> value (mg/kg) was used to determine the reference substance's predicted toxicity category.

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## **Appendix J-1**

### **3T3 NRU Predictions: RC Millimole Regression**

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## 3T3 NRU Predictions: RC Millimole Regression

RC Millimole Regression:  $\text{Log LD}_{50} (\text{mmol/kg}) = 0.435 \log \text{IC}_{50} (\text{mM}) + 0.625$ 

Chemical <sup>a</sup>	Log Observed LD <sub>50</sub> (mmol/kg) <sup>1</sup>	3T3 Log IC <sub>50</sub> (mM) <sup>2</sup>	Log Predicted LD <sub>50</sub> (mmol/kg) <sup>3</sup>	Log Observed LD <sub>50</sub> - Log Predicted LD <sub>50</sub> (mmol/kg)	Outlier <sup>4</sup>	Observed LD <sub>50</sub> (mg/kg) <sup>5</sup>	3T3 IC <sub>50</sub> (ug/mL) <sup>3</sup>	Predicted LD <sub>50</sub> (mg/kg) <sup>6</sup>	Observed LD <sub>50</sub> - Predicted LD <sub>50</sub> (mg/kg)	Observed Toxicity Category <sup>7</sup> (mg/kg)	Predicted Toxicity Category <sup>7</sup> (mg/kg)
Acetaminophen	1.20	-0.501	0.407	0.795	Positive	2404	47.7	386	2018	2000-5000	300-2000
Acetonitrile	1.97	2.29	1.62	0.346		3798	7951	1711	2087	2000-5000	300-2000
Acetylsalicylic acid	0.744	0.574	0.875	-0.131		1000	676	1351	-351	300-2000	300-2000
Aminopterin	-2.17	-4.85	-1.48	-0.683		3.00	0.006	14.5	-11.5	< 5	5-50
5-Aminosalicylic acid	1.70	1.04	1.08	0.628		7749	1667	1824	5925	> 5000	300-2000
Arsenic II trioxide	-1.00	-2.00	-0.246	-0.754	Negative	19.8	1.96	112	-92.4	5-50	50-300
Boric acid	1.63	1.48	1.27	0.367		2660	1850	1144	1516	2000-5000	300-2000
Busulfan	-2.09	-0.501	0.407	-2.50	Negative	2.00	77.7	629	-627	< 5	300-2000
Cadmium II chloride	-0.319	-2.55	-0.484	0.165		88.0	0.518	60.2	27.8	50-300	50-300
Chloramphenicol	1.02	-0.402	0.450	0.571		3393	128	911	2482	2000-5000	300-2000
Citric acid	1.19	0.617	0.894	0.300		3000	796	1503	1497	2000-5000	300-2000
Cupric sulfate pentahydrate	0.080	-0.773	0.289	-0.209		300	42.1	486	-186	50-300	300-2000
Cycloheximide	-2.15	-3.18	-0.757	-1.39	Negative	2.00	0.187	49.3	-47.3	< 5	5-50
Dibutyl phthalate	1.63	-0.748	0.300	1.33	Positive	11998	49.7	555	11443	> 5000	300-2000
Diethyl phthalate	1.59	-0.316	0.487	1.10	Positive	8602	107	683	7919	> 5000	300-2000
Digoxin	-1.64	-0.225	0.527	-2.16	Negative	18.0	466	2630	-2612	5-50	2000-5000
Dimethylformamide	1.58	1.85	1.43	0.152		2800	5224	1974	826	2000-5000	300-2000
Diquat dibromide monohydrate	-0.173	-1.65	-0.094	-0.079		243	8.04	291	-48.3	50-300	50-300
Ethanol	2.48	2.15	1.56	0.922	Positive	14008	6523	1675	12333	> 5000	300-2000
Ethylene glycol	2.14	2.59	1.75	0.387		8567	24317	3515	5052	> 5000	2000-5000
Gibberellic acid	1.26	1.35	1.21	0.047		6305	7810	5664	640	> 5000	> 5000
Glycerol	2.14	2.43	1.68	0.458		12691	24655	4418	8273	> 5000	2000-5000
Hexachlorophene	-0.824	-1.99	-0.239	-0.585		61.0	4.19	235	-174	50-300	50-300
Lactic acid	1.62	1.53	1.29	0.327		3730	3044	1757	1973	2000-5000	300-2000
Lithium I carbonate	1.21	0.881	1.01	0.198		1187	562	753	434	300-2000	300-2000
Meprobamate	0.561	0.376	0.789	-0.228		794	519	1342	-548	300-2000	300-2000
Mercury II chloride	-2.43	-1.82	-0.166	-2.27	Negative	1.00	4.12	185	-184	<5	50-300
Phenol	0.643	-0.152	0.559	0.085		414	66.3	341	73.3	300-2000	300-2000
Phenylthiourea	-1.71	-0.285	0.501	-2.21	Negative	3.00	79.0	482	-479	< 5	300-2000
Potassium I chloride	1.54	1.68	1.35	0.188		2602	3551	1688	914	2000-5000	300-2000
2-Propanol	1.99	1.78	1.40	0.589		5843	3618	1507	4336	> 5000	300-2000
Propranolol HCl	0.201	-1.33	0.047	0.154		470	13.9	329	141	300-2000	300-2000
Sodium arsenite	-0.501	-2.23	-0.347	-0.154		41.0	0.759	58.5	-17.5	5-50	50-300

## 3T3 NRU Predictions: RC Millimole Regression

Chemical <sup>a</sup>	Log Observed LD <sub>50</sub> (mmol/kg) <sup>1</sup>	3T3 Log IC <sub>50</sub> (mM) <sup>2</sup>	Log Predicted LD <sub>50</sub> (mmol/kg) <sup>3</sup>	Log Observed LD <sub>50</sub> - Log Predicted LD <sub>50</sub> (mmol/kg)	Outlier <sup>4</sup>	Observed LD <sub>50</sub> (mg/kg) <sup>5</sup>	3T3 IC <sub>50</sub> (ug/mL) <sup>3</sup>	Predicted LD <sub>50</sub> (mg/kg) <sup>6</sup>	Observed LD <sub>50</sub> - Predicted LD <sub>50</sub> (mg/kg)	Observed Toxicity Category <sup>7</sup> (mg/kg)	Predicted Toxicity Category <sup>7</sup> (mg/kg)
Sodium chloride	1.71	1.91	1.46	0.255		2998	4730	1666	1332	2000-5000	300-2000
Sodium dichromate dihydrate	-0.719	-2.71	-0.552	-0.167		50.0	0.587	83.6	-33.6	5-50	50-300
Sodium I fluoride	0.632	0.269	0.742	-0.110		180	78.0	232	-51.7	50-300	50-300
Sodium hypochlorite	2.08	1.17	1.13	0.944	Positive	8910	1103	1014	7896	> 5000	300-2000
Sodium oxalate	0.063	-0.550	0.386	-0.322		155	37.7	326	-171	50-300	300-2000
Sodium selenate	-2.07	-0.814	0.271	-2.34	Negative	1.60	29.0	353	-351	< 5	300-2000
Thallium I sulfate	-1.24	-1.94	-0.221	-1.02	Negative	29.0	5.74	304	-275	5-50	300-2000
Trichloroacetic acid	1.49	0.742	0.948	0.538		4999	902	1449	3550	2000-5000	300-2000
1,1,1-Trichloroethane	1.89	2.11	1.54	0.344		10298	17248	4664	5635	> 5000	2000-5000
Triethylenemelamine	-2.31	-2.88	-0.626	-1.68	Negative	1.00	0.272	48.4	-47.4	<5	5-50
Triphenyltin hydroxide	-0.921	-4.33	-1.26	0.337		44.0	0.017	20.3	23.7	5-50	5-50
Valproic acid	1.01	0.803	0.974	0.034		1471	916	1359	112	300-2000	300-2000
Xylene	1.61	0.832	0.987	0.621		4300	721	1030	3270	2000-5000	300-2000

<sup>a</sup>Three chemicals were excluded because no rat oral LD<sub>50</sub> was identified: epinephrine bitartrate, colchicine, and propylparaben. Carbon tetrachloride and methanol were excluded because IC<sub>50</sub> values could not be determined. Twenty-one chemicals were excluded based on their mechanisms of action: amitriptyline HCl, atropine sulfate, caffeine, carbamazepine, chloral hydrate, dichlorvos, disulfoton, endosulfan, fenpropothrin, glutethimide, haloperidol, lindane, nicotine, paraquat, parathion, phenobarbital, physostigmine, potassium cyanide, procainamide HCl, strychnine, and verapamil HCl (see Section 6, Table 6-3)

<sup>1</sup>original RC LD<sub>50</sub> values came largely from the 1983/84 RTECS®. Values for non RC chemicals came from current RTECS® and Hazardous Substances Data Bank.

<sup>2</sup>combined 3T3 IC<sub>50</sub> values from three laboratories

<sup>3</sup>LD<sub>50</sub> determined using RC regression: Log LD<sub>50</sub>(mmol/kg) = 0.435 log IC<sub>50</sub> (mM) + 0.625

<sup>4</sup>a difference > 0.699 (or log 5) identifies a chemical as discordant (i.e., an “outlier”)

<sup>5</sup>converted from mmol/kg to mg/kg

<sup>6</sup>LD<sub>50</sub> in mg/kg converted from results of RC regression

<sup>7</sup>Globally Harmonized System (GHS) hazard classification:

Category	Oral LD <sub>50</sub> Limits
1	LD <sub>50</sub> ≤ 5 mg/kg
2	5 < LD <sub>50</sub> ≤ 50 mg/kg
3	50 < LD <sub>50</sub> ≤ 300 mg/kg
4	300 < LD <sub>50</sub> ≤ 2000 mg/kg
5	2000 < LD <sub>50</sub> ≤ 5000 mg/kg
Unclassified	LD <sub>50</sub> > 5000 mg/kg

## **Appendix J-2**

### **3T3 NRU Predictions: 3T3 Combined-Laboratory Regression**

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## 3T3 NRU Predictions: 3T3 Combined-Laboratory Regression

3T3 Combined-Laboratory Regression:  $\text{Log LD}_{50} \text{ (mmol/kg)} = 0.589 \text{ log IC}_{50} \text{ (mM)} + 0.425$ 

Chemical <sup>a</sup>	Log Observed LD <sub>50</sub> (mmol/kg) <sup>1</sup>	3T3 Log IC <sub>50</sub> (mM) <sup>2</sup>	Log Predicted LD <sub>50</sub> (mmol/kg) <sup>3</sup>	Log Observed LD <sub>50</sub> - Log Predicted LD <sub>50</sub> (mmol/kg)	Statistical Outlier <sup>4</sup>	Observed LD <sub>50</sub> (mg/kg) <sup>5</sup>	3T3 IC <sub>50</sub> (ug/mL) <sup>3</sup>	Predicted LD <sub>50</sub> (mg/kg) <sup>6</sup>	Observed LD <sub>50</sub> - Predicted LD <sub>50</sub> (mg/kg)	Reference Toxicity Category <sup>7</sup> (mg/kg)	Predicted Toxicity Category <sup>7</sup> (mg/kg)
Acetaminophen	1.16	-0.501	0.130	1.03		2162	47.7	204	1958	2000-5000	50-300
Acetonitrile	1.94	2.29	1.77	0.170		3595	7951	2429	1166	2000-5000	2000-5000
Acetylsalicylic acid	0.922	0.574	0.763	0.159		1506	676	1045	461	300-2000	300-2000
Aminopterin	-1.80	-4.85	-2.43	0.632		7.00	0.006	1.63	5.37	5-50	< 5
5-Aminosalicylic acid	1.35	1.04	1.04	0.314		3428	1667	1662	1766	2000-5000	300-2000
Amitriptyline HCl	0.046	-1.65	-0.546	0.592		349	7.05	89.3	260	300-2000	50-300
Arsenic II trioxide	-0.897	-2.00	-0.755	-0.142		25.1	1.96	34.8	-9.68	5-50	5-50
Atropine sulfate	0.071	-0.961	-0.141	0.212		819	76.0	502	317	300-2000	300-2000
Boric acid	1.74	1.48	1.29	0.449		3426	1850	1218	2208	2000-5000	300-2000
Busulfan	-1.31	-0.501	0.130	-1.44		12.1	77.7	332	-320	5-50	300-2000
Cadmium II chloride	-0.132	-2.55	-1.08	0.944		135	0.518	15.4	120	50-300	5-50
Caffeine	0.203	-0.105	0.363	-0.160		310	153	448	-138	300-2000	300-2000
Carbamazepine	1.07	-0.360	0.213	0.862		2807	103	386	2421	2000-5000	300-2000
Chloral hydrate	0.586	0.044	0.451	0.135		638	183	467	171	300-2000	300-2000
Chloramphenicol	1.03	-0.402	0.189	0.845		3490	128	499	2991	2000-5000	300-2000
Citric acid	1.49	0.617	0.789	0.701		5929	796	1181	4748	> 5000	300-2000
Colchicine	-1.43	-4.07	-1.97	0.544		15.0	0.034	4.28	10.7	5-50	< 5
Cupric sulfate pentahydrate	0.279	-0.773	-0.030	0.310		475	42.1	233	242	300-2000	50-300
Cycloheximide	-2.15	-3.18	-1.45	-0.702		2.00	0.187	10.1	-8.08	< 5	5-50
Dibutyl phthalate	1.50	-0.748	-0.016	1.52	Positive	8892	49.7	268	8624	> 5000	50-300
Dichlorvos	-0.576	-1.10	-0.220	-0.356		58.7	17.7	133	-74.4	50-300	50-300
Diethyl phthalate	1.62	-0.316	0.239	1.38		9311	107	385	8926	> 5000	300-2000
Digoxin	-1.44	-0.225	0.293	-1.73	Negative	28.3	466	1532	-1504	5-50	300-2000
Dimethylformamide	1.86	1.85	1.52	0.344		5305	5224	2404	2901	> 5000	2000-5000
Diquat dibromide monohydrate	-0.355	-1.65	-0.549	0.194		160	8.04	102	57.7	50-300	50-300
Disulfoton	-1.74	-0.314	0.240	-1.98	Negative	5.00	133	477	-472	< 5	300-2000
Endosulfan	-1.17	-1.81	-0.639	-0.526		27.8	6.35	93.4	-65.6	5-50	50-300
Epinephrine bitartrate	-1.92	-0.752	-0.018	-1.90	Negative	4.00	59.0	320	-316	< 5	300-2000
Ethanol	2.39	2.15	1.69	0.699		11324	6523	2267	9057	> 5000	2000-5000
Ethylene glycol	2.06	2.59	1.95	0.110		7161	24317	5562	1599	> 5000	> 5000
Fenpropothrin	-0.664	-1.16	-0.258	-0.407		75.7	24.2	193	-117	50-300	50-300
Gibberellic acid	1.24	1.35	1.22	0.019		6039	7810	5775	265	> 5000	> 5000

## 3T3 NRU Predictions: 3T3 Combined-Laboratory Regression

Chemical <sup>a</sup>	Log Observed LD <sub>50</sub> (mmol/kg) <sup>1</sup>	3T3 Log IC <sub>50</sub> (mM) <sup>2</sup>	Log Predicted LD <sub>50</sub> (mmol/kg) <sup>3</sup>	Log Observed LD <sub>50</sub> - Log Predicted LD <sub>50</sub> (mmol/kg)	Statistical Outlier <sup>4</sup>	Observed LD <sub>50</sub> (mg/kg) <sup>5</sup>	3T3 IC <sub>50</sub> (ug/mL) <sup>3</sup>	Predicted LD <sub>50</sub> (mg/kg) <sup>6</sup>	Observed LD <sub>50</sub> - Predicted LD <sub>50</sub> (mg/kg)	Reference Toxicity Category <sup>7</sup> (mg/kg)	Predicted Toxicity Category <sup>7</sup> (mg/kg)
Glutethimide	0.441	-0.095	0.369	0.072		600	174	508	92.0	300-2000	300-2000
Glycerol	2.33	2.43	1.85	0.477		19770	24655	6594	13176	> 5000	> 5000
Haloperidol	-0.057	-1.79	-0.628	0.572		330	6.13	88.5	241	300-2000	50-300
Hexachlorophene	-0.696	-1.99	-0.745	0.050		82.0	4.19	73.2	8.84	50-300	50-300
Lactic acid	1.61	1.53	1.33	0.280		3635	3044	1906	1729	2000-5000	300-2000
Lindane	-0.464	-0.432	0.171	-0.634		100	108	431	-331	50-300	300-2000
Lithium I carbonate	0.902	0.881	0.944	-0.042		590	562	649	-59.2	300-2000	300-2000
Meprobamate	0.803	0.376	0.646	0.156		1387	519	967	420	300-2000	300-2000
Mercury II chloride	-0.830	-1.82	-0.646	-0.183		40.2	4.12	61.3	-21.1	5-50	50-300
Nicotine	-0.367	0.347	0.630	-1.00		69.7	361	691	-622	50-300	300-2000
Paraquat	-0.443	-1.11	-0.227	-0.217		92.7	20.1	153	-59.9	50-300	50-300
Parathion	-1.68	-0.891	-0.100	-1.58	Negative	6.10	37.4	231	-225	5-50	50-300
Phenobarbital	-0.016	0.392	0.656	-0.672		224	573	1052	-828	50-300	300-2000
Phenol	0.908	-0.152	0.335	0.573		762	66.3	204	558	300-2000	50-300
Phenylthiourea	-1.71	-0.285	0.257	-1.96	Negative	3.00	79.0	275	-272	< 5	50-300
Physostigmine	-1.74	-1.03	-0.181	-1.56	Negative	5.00	25.8	182	-177	< 5	50-300
Potassium I chloride	1.58	1.68	1.41	0.162		2802	3551	1931	871	2000-5000	300-2000
Potassium cyanide	-0.956	-0.274	0.264	-1.22		7.20	34.6	119	-112	5-50	50-300
Procainamide HCl	0.856	0.210	0.549	0.307		1950	441	961	989	300-2000	300-2000
2-Propanol	1.93	1.78	1.47	0.456		5105	3618	1787	3318	> 5000	300-2000
Propranolol HCl	0.197	-1.33	-0.358	0.555		466	13.9	130	336	300-2000	50-300
Propylparaben	1.55	-0.84	-0.069	1.62	Positive	6332	26.1	154	6178	> 5000	50-300
Sodium arsenite	-0.474	-2.23	-0.891	0.416		43.6	0.759	16.7	26.9	5-50	5-50
Sodium chloride	1.84	1.91	1.55	0.292		4050	4730	2068	1982	2000-5000	2000-5000
Sodium dichromate dihydrate	-0.771	-2.71	-1.17	0.398		50.5	0.587	20.2	30.3	50-300	5-50
Sodium I fluoride	0.480	0.269	0.583	-0.104		127	78.0	161	-34.1	50-300	50-300
Sodium hypochlorite	2.14	1.17	1.11	1.03		10328	1103	969	9359	> 5000	300-2000
Sodium oxalate	0.674	-0.550	0.101	0.573		633	37.7	169	464	300-2000	50-300
Sodium selenate	-1.80	-0.814	-0.054	-1.74	Negative	3.00	29.0	167	-164	< 5	50-300
Strychnine	-1.72	-0.326	0.233	-1.96	Negative	6.30	158	572	-566	5-50	300-2000
Thallium I sulfate	-1.31	-1.94	-0.720	-0.585		25.0	5.74	96.2	-71.2	5-50	50-300
Trichloroacetic acid	1.28	0.742	0.862	0.420		3127	902	1189	1938	2000-5000	300-2000
1,1,1-Trichloroethane	1.96	2.11	1.67	0.288		12078	17248	6222	5857	> 5000	> 5000

## 3T3 NRU Predictions: 3T3 Combined-Laboratory Regression

Chemical <sup>a</sup>	Log Observed LD <sub>50</sub> (mmol/kg) <sup>1</sup>	3T3 Log IC <sub>50</sub> (mM) <sup>2</sup>	Log Predicted LD <sub>50</sub> (mmol/kg) <sup>3</sup>	Log Observed LD <sub>50</sub> - Log Predicted LD <sub>50</sub> (mmol/kg)	Statistical Outlier <sup>4</sup>	Observed LD <sub>50</sub> (mg/kg) <sup>5</sup>	3T3 IC <sub>50</sub> (ug/mL) <sup>3</sup>	Predicted LD <sub>50</sub> (mg/kg) <sup>6</sup>	Observed LD <sub>50</sub> - Predicted LD <sub>50</sub> (mg/kg)	Reference Toxicity Category <sup>7</sup> (mg/kg)	Predicted Toxicity Category <sup>7</sup> (mg/kg)
Triethylenemelamine	-1.71	-2.88	-1.27	-0.440		4.00	0.272	11.0	-7.01	< 5	5-50
Triphenyltin hydroxide	-0.047	-4.33	-2.12	2.08	Positive	329	0.017	2.75	326	300-2000	< 5
Valproic acid	0.839	0.803	0.898	-0.059		996	916	1140	-144	300-2000	300-2000
Verapamil HCl	-0.646	-1.15	-0.251	-0.395		111	34.9	275	-164	50-300	50-300
Xylene	1.64	0.832	0.915	0.728		4665	721	873	3792	2000-5000	300-2000

<sup>a</sup>carbon tetrachloride and methanol were excluded because IC<sub>50</sub> values could not be determined.<sup>1</sup>reference LD<sub>50</sub> values that were collected from the literature<sup>2</sup>combined 3T3 IC<sub>50</sub> values from three laboratories<sup>3</sup>LD<sub>50</sub> determined using regression: Log LD<sub>50</sub> (mmol/kg) = 0.589 log IC<sub>50</sub> (mM) + 0.425<sup>4</sup>outlier range = 1.510 - 1.573 (90% prediction interval)<sup>5</sup>converted from mmol/kg to mg/kg<sup>6</sup>LD<sub>50</sub> in mg/kg converted from results of regression<sup>7</sup>Globally Harmonized System (GHS) hazard classification:

Category	Oral LD <sub>50</sub> Limits
1	LD <sub>50</sub> ≤ 5 mg/kg
2	5 < LD <sub>50</sub> ≤ 50 mg/kg
3	50 < LD <sub>50</sub> ≤ 300 mg/kg
4	300 < LD <sub>50</sub> ≤ 2000 mg/kg
5	2000 < LD <sub>50</sub> ≤ 5000 mg/kg
Unclassified	LD <sub>50</sub> > 5000 mg/kg

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## **Appendix J-3**

### **NHK NRU Predictions: RC Millimole Regression**

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## NHK NRU Predictions: RC Millimole Regression

RC Millimole Regression:  $\text{Log LD}_{50} (\text{mmol/kg}) = 0.435 \text{ log IC}_{50} (\text{mM}) + 0.625$ 

Chemical	Log Observed LD <sub>50</sub> (mmol/kg) <sup>1</sup>	NHK Log IC <sub>50</sub> (mM) <sup>2</sup>	Log Predicted LD <sub>50</sub> (mmol/kg) <sup>3</sup>	Log Observed LD <sub>50</sub> - Log Predicted LD <sub>50</sub> (mmol/kg)	Statistical Outlier <sup>4</sup>	Observed LD <sub>50</sub> (mg/kg) <sup>5</sup>	NHK IC <sub>50</sub> (ug/mL) <sup>3</sup>	Predicted LD <sub>50</sub> (mg/kg) <sup>6</sup>	Observed LD <sub>50</sub> - Predicted LD <sub>50</sub> (mg/kg)	Observed Toxicity Category <sup>7</sup> (mg/kg)	Predicted Toxicity Category <sup>7</sup> (mg/kg)
Acetaminophen	1.20	0.535	0.858	0.344		2404	518	1089	1315	2000-5000	300-2000
Acetonitrile	1.97	2.37	1.65	0.312		3798	9528	1851	1947	2000-5000	300-2000
Acetylsalicylic acid	0.744	0.526	0.854	-0.110		1000	605	1287	-287	300-2000	300-2000
Aminopterin	-2.17	0.182	0.704	-2.87	Negative	3.00	669	2228	-2225	< 5	2000-5000
5-Aminosalicylic acid	1.70	-0.516	0.401	1.30	Positive	7749	46.7	385	7364	> 5000	300-2000
Arsenic II trioxide	-1.00	-1.58	-0.060	-0.940	Negative	19.8	5.26	172	-152	5-50	50-300
Boric acid	1.63	0.833	0.988	0.646		2660	421	601	2059	2000-5000	300-2000
Busulfan	-2.09	0.024	0.635	-2.73	Negative	2.00	260	1064	-1062	< 5	300-2000
Cadmium II chloride	-0.319	-2.00	-0.244	-0.075		88.0	1.84	105	-16.5	50-300	50-300
Chloramphenicol	1.02	0.033	0.639	0.382		3393	348	1408	1985	2000-5000	300-2000
Citric acid	1.19	0.318	0.763	0.430		3000	400	1114	1886	2000-5000	300-2000
Cupric sulfate pentahydrate	0.080	-0.104	0.580	-0.500		300	197	949	-649	50-300	300-2000
Cycloheximide	-2.15	-3.58	-0.934	-1.21	Negative	2.00	0.073	32.8	-30.8	< 5	5-50
Dibutyl phthalate	1.63	-0.987	0.196	1.44	Positive	11998	28.7	437	11561	> 5000	300-2000
Diethyl phthalate	1.59	-0.266	0.509	1.08	Positive	8602	120	718	7884	> 5000	300-2000
Digoxin	-1.64	-5.89	-1.94	0.299		18.0	0.001	9.04	8.96	5-50	5-50
Dimethylformamide	1.58	2.03	1.51	0.077		2800	7760	2345	455	2000-5000	2000-5000
Diquat dibromide monohydrate	-0.173	-1.91	-0.205	0.032		243	4.48	226	17.2	50-300	50-300
Ethanol	2.48	2.34	1.64	0.841	Positive	14008	10018	2019	11989	> 5000	2000-5000
Ethylene glycol	2.14	2.83	1.86	0.284		8567	41852	4451	4116	> 5000	2000-5000
Gibberellic acid	1.26	0.916	1.02	0.237		6305	2856	3657	2648	> 5000	2000-5000
Glycerol	2.14	2.43	1.96	0.175		12691	24730	8481	4211	> 5000	> 5000
Hexachlorophene	-0.824	-4.15	-1.18	0.356		61.0	0.029	26.9	34.1	50-300	5-50
Lactic acid	1.62	1.16	1.13	0.487		3730	1304	1215	2515	2000-5000	300-2000
Lithium II carbonate	1.21	0.801	0.974	0.232		1187	468	695	492	300-2000	300-2000
Meprobamate	0.561	0.213	0.718	-0.157		794	357	1140	-346	300-2000	300-2000
Mercury II chloride	-2.43	-1.67	-0.102	-2.33	Negative	1.00	5.80	215	-214	<5	50-300
Methanol	2.61	1.68	1.36	1.25	Positive	13012	1529	726	12286	> 5000	300-2000
Phenol	0.643	-0.098	0.582	0.061		414	75.0	360	54	300-2000	300-2000
Phenylthiourea	-1.71	0.344	0.775	-2.48	Negative	3.00	336	906	-903	< 5	300-2000
Potassium I chloride	1.54	1.48	1.27	0.275		2602	2237	1381	1221	2000-5000	300-2000

## NHK NRU Predictions: RC Millimole Regression

Chemical	Log Observed LD <sub>50</sub> (mmol/kg) <sup>1</sup>	NHK Log IC <sub>50</sub> (mM) <sup>2</sup>	Log Predicted LD <sub>50</sub> (mmol/kg) <sup>3</sup>	Log Observed LD <sub>50</sub> - Log Predicted LD <sub>50</sub> (mmol/kg)	Statistical Outlier <sup>4</sup>	Observed LD <sub>50</sub> (mg/kg) <sup>5</sup>	NHK IC <sub>50</sub> (ug/mL) <sup>3</sup>	Predicted LD <sub>50</sub> (mg/kg) <sup>6</sup>	Observed LD <sub>50</sub> - Predicted LD <sub>50</sub> (mg/kg)	Observed Toxicity Category <sup>7</sup> (mg/kg)	Predicted Toxicity Category <sup>7</sup> (mg/kg)
2-Propanol	1.99	1.95	1.47	0.514		5843	5364	1788	4055	> 5000	300-2000
Propranolol HCl	0.201	-0.923	0.224	-0.023		470	35.3	495	-25.0	300-2000	300-2000
Sodium arsenite	-0.501	-2.44	-0.434	-0.066		41.0	0.477	47.8	-6.78	5-50	5-50
Sodium chloride	1.71	1.53	1.29	0.418		2998	1997	1145	1853	2000-5000	300-2000
Sodium dichromate dihydrate	-0.719	-2.62	-0.513	-0.206		56.9	0.721	91.4	-34.6	50-300	50-300
Sodium I fluoride	0.632	0.074	0.657	-0.025		180	49.8	191	-10.6	50-300	50-300
Sodium hypochlorite	2.08	1.30	1.19	0.885	Positive	8910	1502	1160	7750	> 5000	300-2000
Sodium oxalate	0.063	0.400	0.799	-0.736	Negative	155	337	844	-689	50-300	300-2000
Sodium selenate	-2.07	-1.27	0.074	-2.15	Negative	1.60	10.2	224	-222	< 5	50-300
Thallium I sulfate	-1.24	-3.52	-0.907	-0.333		29.0	0.152	62.5	-33.5	5-50	50-300
Trichloroacetic acid	1.49	0.403	0.800	0.685		4999	413	1032	3967	2000-5000	300-2000
1,1,1-Trichloroethane	1.89	1.78	1.40	0.486		10298	8122	3361	6938	> 5000	2000-5000
Triethylenemelamine	-2.31	-2.04	-0.263	-2.05	Negative	1.00	1.85	111	-110	<5	50-300
Triphenyltin hydroxide	-0.921	-4.56	-1.36	0.438		44.0	0.010	16.0	28.0	5-50	5-50
Valproic acid	1.01	0.550	0.864	0.144		1471	512	1055	416	300-2000	300-2000
Xylene	1.61	0.642	0.904	0.703	Positive	4300	466	852	3448	2000-5000	300-2000

<sup>a</sup>Three chemicals were excluded because no rat LD<sub>50</sub> was identified: epinephrine bitartrate, colchicine, and propylparaben. Carbon tetrachloride and methanol were excluded because IC<sub>50</sub> values could not be determined. Twenty-one chemicals were excluded based on their mechanisms of action: amitriptyline HCl, atropine sulfate, caffeine, carbamazepine, chloral hydrate, dichlorvos, disulfoton, endosulfan, fenpropothrin, glutethimide, haloperidol, lindane, nicotine, paraquat, parathion, phenobarbital, physostigmine, potassium cyanide, procainamide HCl, strychnine, and verapamil HCl (see **Section 6, Table 6-3**).

<sup>1</sup>original RC LD<sub>50</sub> values came largely from the 1983/84 RTECS®. Values for nonRC chemicals came from current RTECS® and Hazardous Substances Data Bank.

<sup>2</sup>combined NHK IC<sub>50</sub> values from three laboratories

<sup>3</sup>LD<sub>50</sub> determined using RC regression: Log LD<sub>50</sub>(mmol/kg) = 0.435 log IC<sub>50</sub> (mM) + 0.625

<sup>4</sup>a difference > 0.699 (or log 5) identifies a chemical as discordant (i.e.. an “outlier”)

<sup>5</sup>converted from mmol/kg to mg/kg

<sup>6</sup>LD<sub>50</sub> in mg/kg converted from results of RC regression

<sup>7</sup>Globally Harmonized System (GHS) hazard classification:

Category	Oral LD <sub>50</sub> Limits
1	LD <sub>50</sub> ≤ 5 mg/kg
2	5 < LD <sub>50</sub> ≤ 50 mg/kg
3	50 < LD <sub>50</sub> ≤ 300 mg/kg
4	300 < LD <sub>50</sub> ≤ 2000 mg/kg
5	2000 < LD <sub>50</sub> ≤ 5000 mg/kg
Unclassified	LD <sub>50</sub> > 5000 mg/kg

## **Appendix J-4**

### **NHK NRU Predictions: NHK Combined-Laboratory Regression**

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## NHK NRU Predictions: NHK Combined-Laboratory Regression

NHK Combined-Laboratory Regression:  $\text{Log LD}_{50} \text{ (mmol/kg)} = 0.510 \text{ log IC}_{50} \text{ (mM)} + 0.452$ 

Chemical <sup>a</sup>	Log Observed LD <sub>50</sub> (mmol/kg) <sup>1</sup>	NHK Log IC <sub>50</sub> (mM) <sup>2</sup>	Log Predicted LD <sub>50</sub> (mmol/kg) <sup>3</sup>	Log Observed LD <sub>50</sub> - Log Predicted LD <sub>50</sub> (mmol/kg)	Statistical Outlier <sup>4</sup>	Observed LD <sub>50</sub> (mg/kg) <sup>5</sup>	NHK IC <sub>50</sub> (ug/mL) <sup>3</sup>	Predicted LD <sub>50</sub> (mg/kg) <sup>6</sup>	Observed LD <sub>50</sub> - Predicted LD <sub>50</sub> (mg/kg)	Observed Toxicity Category <sup>7</sup> (mg/kg)	Predicted Toxicity Category <sup>7</sup> (mg/kg)
Acetaminophen	1.16	0.535	0.725	0.431		2162	518	802	1360	2000-5000	300-2000
Acetonitrile	1.94	2.37	1.66	0.284		3595	9528	1870	1725	2000-5000	300-2000
Acetylsalicylic acid	0.922	0.526	0.720	0.202		1506	605	947	559	300-2000	300-2000
Aminopterin	-1.80	0.182	0.545	-2.34	Negative	7.00	669	1543	-1536	5-50	300-2000
5-Aminosalicylic acid	1.35	-0.516	0.189	1.16		3428	46.7	237	3191	2000-5000	50-300
Amitriptyline HCl	0.046	-1.54	-0.336	0.382		349	8.96	145	204	300-2000	50-300
Arsenic II trioxide	-0.897	-1.58	-0.351	-0.545		25.1	5.26	88.1	-63.0	5-50	50-300
Atropine sulfate	0.071	-0.929	-0.022	0.093		819	81.8	661	158	300-2000	300-2000
Boric acid	1.74	0.833	0.877	0.867		3426	421	466	2960	2000-5000	300-2000
Busulfan	-1.31	0.024	0.464	-1.77	Negative	12.1	260	717	-705	5-50	300-2000
Cadmium II chloride	-0.132	-2.00	-0.567	0.435		135	1.84	49.7	85.5	50-300	50-300
Caffeine	0.203	0.516	0.715	-0.512		310	638	1008	-698	300-2000	300-2000
Carbamazepine	1.07	-0.453	0.221	0.854		2807	83.2	393	2414	2000-5000	300-2000
Chloral hydrate	0.586	-0.094	0.404	0.182		638	133	419	219	300-2000	300-2000
Chloramphenicol	1.03	0.033	0.469	0.565		3490	348	951	2539	2000-5000	300-2000
Citric acid	1.49	0.318	0.614	0.875		5929	400	790	5139	> 5000	300-2000
Colchicine	-1.43	-4.78	-1.99	0.560		15.0	0.01	4.13	10.9	5-50	< 5
Cupric sulfate pentahydrate	0.279	-0.104	0.399	-0.120		475	197	626	-151	300-2000	300-2000
Cycloheximide	-2.15	-3.58	-1.38	-0.773		2.00	0.073	11.9	-9.85	< 5	5-50
Dibutyl phthalate	1.50	-0.987	-0.051	1.56		8892	28.7	247	8645	> 5000	50-300
Dichlorvos	-0.576	-1.32	-0.219	-0.357		58.7	10.7	134	-74.8	50-300	50-300
Diethyl phthalate	1.62	-0.266	0.316	1.31		9311	120	460	8851	> 5000	300-2000
Digoxin	-1.44	-5.89	-2.55	1.11		28.3	0.001	2.19	26.1	5-50	< 5
Dimethylformamide	1.86	2.03	1.49	0.376		5305	7760	2234	3071	> 5000	2000-5000
Diquat dibromide monohydrate	-0.355	-1.91	-0.521	0.166		160	4.48	109	50.9	50-300	50-300
Disulfoton	-1.74	-0.007	0.448	-2.19	Negative	5.00	270	770	-765	< 5	300-2000
Endosulfan	-1.17	-2.28	-0.712	-0.454		27.8	2.13	79.0	-51.2	5-50	50-300
Epinephrine bitartrate	-1.92	-0.581	0.156	-2.08	Negative	4.00	87.4	477	-473	< 5	300-2000
Ethanol	2.39	2.34	1.64	0.747		11324	10018	2030	9294	> 5000	2000-5000
Ethylene glycol	2.06	2.83	1.89	0.167		7161	41852	4871	2290	> 5000	2000-5000
Fenpropothrin	-0.664	-2.16	-0.649	-0.016		75.7	2.43	78.5	-2.75	50-300	50-300
Gibberellic acid	1.24	0.916	0.919	0.322		6039	2856	2876	3163	> 5000	2000-5000

## NHK NRU Predictions: NHK Combined-Laboratory Regression

Chemical <sup>a</sup>	Log Observed LD <sub>50</sub> (mmol/kg) <sup>1</sup>	NHK Log IC <sub>50</sub> (mM) <sup>2</sup>	Log Predicted LD <sub>50</sub> (mmol/kg) <sup>3</sup>	Log Observed LD <sub>50</sub> - Log Predicted LD <sub>50</sub> (mmol/kg)	Statistical Outlier <sup>4</sup>	Observed LD <sub>50</sub> (mg/kg) <sup>5</sup>	NHK IC <sub>50</sub> (ug/mL) <sup>3</sup>	Predicted LD <sub>50</sub> (mg/kg) <sup>6</sup>	Observed LD <sub>50</sub> - Predicted LD <sub>50</sub> (mg/kg)	Observed Toxicity Category <sup>7</sup> (mg/kg)	Predicted Toxicity Category <sup>7</sup> (mg/kg)
Glutethimide	0.441	-0.098	0.402	0.039		600	174	549	51.4	300-2000	300-2000
Glycerol	2.33	2.43	1.69	0.641		19770	24730	4519	15251	> 5000	2000-5000
Haloperidol	-0.057	-2.05	-0.593	0.536		330	3.36	95.9	234	300-2000	50-300
Hexachlorophene	-0.696	-4.15	-1.66	0.968		82.0	0.029	8.82	73.2	50-300	5-50
Lactic acid	1.61	1.16	1.04	0.562		3635	1304	997	2638	2000-5000	300-2000
Lindane	-0.464	-1.19	-0.155	-0.308		100	18.7	203	-103	50-300	50-300
Lithium I carbonate	0.902	0.801	0.861	0.042		590	468	536	53.9	300-2000	300-2000
Meprobamate	0.803	0.213	0.561	0.242		1387	357	794	593	300-2000	300-2000
Mercury II chloride	-0.830	-1.67	-0.400	-0.430		40.2	5.80	108	-67.9	5-50	50-300
Methanol	2.43	1.68	1.31	1.13		8710	1529	651	8058	> 5000	300-2000
Nicotine	-0.367	-0.182	0.359	-0.726		69.7	107	371	-301	50-300	300-2000
Paraquat	-0.443	-0.621	0.135	-0.579		92.7	61.6	351	-259	50-300	300-2000
Parathion	-1.68	-0.983	-0.050	-1.63		6.10	30.3	260	-254	5-50	50-300
Phenobarbital	-0.016	0.285	0.597	-0.613		224	448	919	-695	50-300	300-2000
Phenol	0.908	-0.098	0.402	0.507		762	75.0	237	525	300-2000	50-300
Phenylthiourea	-1.71	0.344	0.628	-2.33	Negative	3.00	336	646	-643	< 5	300-2000
Physostigmine	-1.74	-0.493	0.201	-1.94	Negative	5.00	88.5	437	-432	< 5	300-2000
Potassium I chloride	1.58	1.48	1.21	0.370		2802	2237	1196	1606	2000-5000	300-2000
Potassium cyanide	-0.956	-0.352	0.272	-1.23		7.20	29.0	122	-115	5-50	50-300
Procainamide HCl	0.856	0.807	0.863	-0.008		1950	1741	1984	-34.4	300-2000	300-2000
2-Propanol	1.93	1.95	1.45	0.482		5105	5364	1682	3423	> 5000	300-2000
Propranolol HCl	0.197	-0.923	-0.019	0.216		466	35.3	283	183	300-2000	50-300
Propylparaben	1.55	-1.04	-0.076	1.62		6332	16.6	151	6181	> 5000	50-300
Sodium arsenite	-0.474	-2.44	-0.790	0.316		43.6	0.477	21.1	22.5	5-50	5-50
Sodium chloride	1.84	1.53	1.23	0.607		4050	1997	1002	3048	2000-5000	300-2000
Sodium dichromate dihydrate	-0.771	-2.62	-0.882	0.111		50.5	0.721	39.1	11.4	50-300	5-50
Sodium I fluoride	0.480	0.074	0.490	-0.010		127	49.8	130	-2.91	50-300	50-300
Sodium hypochlorite	2.14	1.30	1.12	1.02		10328	1502	976	9352	> 5000	300-2000
Sodium oxalate	0.674	0.400	0.656	0.018		633	337	607	25.8	300-2000	300-2000
Sodium selenate	-1.80	-1.27	-0.194	-1.61		3.00	10.2	121	-118	< 5	50-300
Strychnine	-1.72	-0.729	0.080	-1.81	Negative	6.30	62.5	402	-396	5-50	300-2000
Thallium I sulfate	-1.31	-3.52	-1.34	0.039		25.0	0.152	22.8	2.16	5-50	5-50
Trichloroacetic acid	1.28	0.403	0.658	0.624		3127	413	743	2384	2000-5000	300-2000

## NHK NRU Predictions: NHK Combined-Laboratory Regression

Chemical <sup>a</sup>	Log Observed LD <sub>50</sub> (mmol/kg) <sup>1</sup>	NHK Log IC <sub>50</sub> (mM) <sup>2</sup>	Log Predicted LD <sub>50</sub> (mmol/kg) <sup>3</sup>	Log Observed LD <sub>50</sub> - Log Predicted LD <sub>50</sub> (mmol/kg)	Statistical Outlier <sup>4</sup>	Observed LD <sub>50</sub> (mg/kg) <sup>5</sup>	NHK IC <sub>50</sub> (ug/mL) <sup>3</sup>	Predicted LD <sub>50</sub> (mg/kg) <sup>6</sup>	Observed LD <sub>50</sub> - Predicted LD <sub>50</sub> (mg/kg)	Observed Toxicity Category <sup>7</sup> (mg/kg)	Predicted Toxicity Category <sup>7</sup> (mg/kg)
1,1,1-Trichloroethane	1.96	1.78	1.36	0.595		12078	8122	3071	9007	> 5000	2000-5000
Triethylenemelamine	-1.71	-2.04	-0.590	-1.12		4.00	1.85	52.5	-48.5	< 5	50-300
Triphenyltin hydroxide	-0.047	-4.56	-1.87	1.83	Positive	329	0.010	4.90	324	300-2000	< 5
Valproic acid	0.839	0.550	0.733	0.107		996	512	779	217	300-2000	300-2000
Verapamil HCl	-0.646	-0.869	0.009	-0.655		111	66.5	501	-390	50-300	300-2000
Xylene	1.64	0.642	0.779	0.863		4665	466	639	4026	2000-5000	300-2000

<sup>a</sup>carbon tetrachloride was excluded because IC<sub>50</sub> values could not be determined.<sup>1</sup>reference LD<sub>50</sub> values that were collected from the literature<sup>2</sup>combined NHK IC<sub>50</sub> values from three laboratories<sup>3</sup>LD<sub>50</sub> determined using regression: Log LD<sub>50</sub> (mmol/kg) = 0.510 log IC<sub>50</sub> (mM) + 0.452<sup>4</sup>outlier range = 1.639 - 1.701 (90% prediction interval)<sup>5</sup>converted from mmol/kg to mg/kg<sup>6</sup>LD<sub>50</sub> in mg/kg converted from results of regression<sup>7</sup>Globally Harmonized System (GHS) hazard classification:

Category	Oral LD <sub>50</sub> Limits
1	LD <sub>50</sub> ≤ 5 mg/kg
2	5 < LD <sub>50</sub> ≤ 50 mg/kg
3	50 < LD <sub>50</sub> ≤ 300 mg/kg
4	300 < LD <sub>50</sub> ≤ 2000 mg/kg
5	2000 < LD <sub>50</sub> ≤ 5000 mg/kg
Unclassified	LD <sub>50</sub> > 5000 mg/kg

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## **Appendix J-5**

### **3T3 NRU Predictions: RC Rat-Only Weight Regression**

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## 3T3 NRU Predictions: RC Rat-Only Weight Regression

RC Rat-Only Weight Regression: Log LD<sub>50</sub> (mg/kg) = 0.372 log IC<sub>50</sub> (ug/mL) + 2.024

Chemical <sup>a</sup>	Log Observed LD <sub>50</sub> (mg/kg) <sup>1</sup>	3T3 Log IC <sub>50</sub> (ug/mL) <sup>2</sup>	Log Predicted LD <sub>50</sub> (mg/kg) <sup>3</sup>	Observed LD <sub>50</sub> (mg/kg) <sup>1</sup>	3T3 IC <sub>50</sub> (ug/mL) <sup>2</sup>	Predicted LD <sub>50</sub> (mg/kg) <sup>3</sup>	Observed LD <sub>50</sub> - Predicted LD <sub>50</sub> (mg/kg)	Observed Toxicity Category <sup>4</sup> (mg/kg)	Predicted Toxicity Category <sup>4</sup> (mg/kg)
Acetaminophen	3.33	1.68	2.65	2162	47.7	445	1717	2000-5000	300-2000
Acetonitrile	3.56	3.90	3.47	3595	7951	2985	610	2000-5000	2000-5000
Acetylsalicylic acid	3.18	2.83	3.08	1506	676	1194	312	300-2000	300-2000
Aminopterin	0.845	-2.20	1.20	7.00	0.006	16.0	-9.00	5-50	5-50
5-Aminosalicylic acid	3.54	3.22	3.22	3428	1667	1669	1759	2000-5000	300-2000
Arsenic III trioxide	1.40	0.293	2.13	25.1	1.96	136	-111	5-50	50-300
Boric acid	3.53	3.27	3.24	3426	1850	1735	1691	2000-5000	300-2000
Busulfan	1.08	1.89	2.73	12.1	77.7	534	-521	5-50	300-2000
Cadmium II chloride	2.13	-0.286	1.92	135	0.518	82.7	52.5	50-300	50-300
Chloramphenicol	3.54	2.11	2.81	3490	128	643	2847	2000-5000	300-2000
Citric acid	3.77	2.90	3.10	5929	796	1268	4661	> 5000	300-2000
Cupric sulfate pentahydrate	2.68	1.62	2.63	475	42.1	425	50.1	300-2000	300-2000
Cycloheximide	0.301	-0.727	1.75	2.00	0.187	56.7	-54.7	< 5	50-300
Dibutyl phthalate	3.95	1.70	2.66	8892	49.7	452	8440	> 5000	300-2000
Diethyl phthalate	3.97	2.03	2.78	9311	107	602	8709	> 5000	300-2000
Digoxin	1.45	2.67	3.02	28.3	466	1039	-1010	5-50	300-2000
Dimethylformamide	3.72	3.72	3.41	5305	5224	2553	2752	> 5000	2000-5000
Diquat dibromide monohydrate	2.20	0.905	2.36	160	8.04	229	-69.5	50-300	50-300
Ethanol	4.05	3.81	3.44	11324	6523	2773	8551	> 5000	2000-5000
Ethylene glycol	3.85	4.39	3.66	7161	24317	4524	2637	> 5000	2000-5000
Gibberellic acid	3.78	3.89	3.47	6039	7810	2965	3074	> 5000	2000-5000
Glycerol	4.30	4.39	3.66	19770	24655	4548	15222	> 5000	2000-5000
Hexachlorophene	1.91	0.623	2.26	82.0	4.19	180	-98.2	50-300	50-300
Lactic acid	3.56	3.48	3.32	3635	3044	2089	1546	2000-5000	2000-5000
Lithium I carbonate	2.77	2.75	3.05	590	562	1114	-524	300-2000	300-2000
Meprobamate	3.14	2.72	3.03	1387	519	1081	305	300-2000	300-2000
Mercury II chloride	1.60	0.615	2.25	40.2	4.12	179	-139	5-50	50-300
Phenol	2.74	1.82	2.70	548	66.3	503	44.6	300-2000	300-2000
Phenylthiourea	0.477	1.90	2.73	3.00	79.0	537	-534	< 5	300-2000
Potassium I chloride	3.45	3.55	3.34	2802	3551	2212	590.2	2000-5000	2000-5000

## 3T3 NRU Predictions: RC Rat-Only Weight Regression

Chemical <sup>a</sup>	Log Observed LD <sub>50</sub> (mg/kg) <sup>1</sup>	3T3 Log IC <sub>50</sub> (ug/mL) <sup>2</sup>	Log Predicted LD <sub>50</sub> (mg/kg) <sup>3</sup>	Observed LD <sub>50</sub> (mg/kg) <sup>1</sup>	3T3 IC <sub>50</sub> (ug/mL) <sup>2</sup>	Predicted LD <sub>50</sub> (mg/kg) <sup>3</sup>	Observed LD <sub>50</sub> - Predicted LD <sub>50</sub> (mg/kg)	Observed Toxicity Category <sup>4</sup> (mg/kg)	Predicted Toxicity Category <sup>4</sup> (mg/kg)
2-Propanol	3.71	3.56	3.35	5105	3618	2227	2878	> 5000	2000-5000
Propranolol HCl	2.67	1.14	2.45	466	14	281	185	300-2000	50-300
Sodium arsenite	1.64	-0.120	1.98	43.6	0.759	95.4	-51.8	5-50	50-300
Sodium chloride	3.61	3.67	3.39	4050	4730	2461	1589	2000-5000	2000-5000
Sodium dichromate dihydrate	1.70	-0.232	1.94	50.5	0.587	86.7	-36.2	50-300	50-300
Sodium hypochlorite	4.01	3.04	3.16	10328	1103	1431	8896	> 5000	300-2000
Sodium I fluoride	2.10	1.89	2.73	127	78.0	534	-408	50-300	300-2000
Sodium oxalate	2.80	1.58	2.61	633	37.7	408	225	300-2000	300-2000
Sodium selenate	0.477	1.46	2.57	3.00	29.0	370	-367	< 5	300-2000
Thallium I sulfate	1.40	0.759	2.31	25.0	5.74	202	-177	5-50	50-300
Trichloroacetic acid	3.72	2.96	3.12	5229	902	1328	3900	> 5000	300-2000
1,1,1-Trichloroethane	4.08	4.24	3.60	12078	17248	3982	8096	> 5000	2000-5000
Triethylenemelamine	0.602	-0.565	1.81	4.00	0.272	65.1	-61.1	< 5	50-300
Triphenyltin Hydroxide	2.52	-1.76	1.37	329	0.017	23.3	306	300-2000	5-50
Valproic acid	3.00	2.96	3.13	996	916	1336	-340	300-2000	300-2000
Xylene	3.67	2.86	3.09	4665	721	1222	3443	2000-5000	300-2000

<sup>a</sup>Three chemicals were excluded because no rat LD<sub>50</sub> was identified: epinephrine bitartrate, colchicine, and propylparaben. Carbon tetrachloride and methanol were excluded because an IC<sub>50</sub> value could not be determined. Twenty-one chemicals were excluded based on their mechanisms of action: amitriptyline HCl, atropine sulfate, caffeine, carbamazepine, chloral hydrate, dichlorvos, disulfoton, endosulfan, fenpropothrin, glutethimide, haloperidol, lindane, nicotine, paraquat, parathion, phenobarbital, physostigmine, potassium cyanide, procainamide HCl, strychnine, and verapamil HCl (see **Section 6, Table 6-3**).

<sup>1</sup> reference LD<sub>50</sub> values that were collected from the literature

<sup>2</sup> combined 3T3 IC<sub>50</sub> values from three laboratories

<sup>3</sup> LD<sub>50</sub> determined using: log LD<sub>50</sub> (mg/kg) = 0.372 log IC<sub>50</sub> ug/mL + 2.024

<sup>4</sup>Globally Harmonized System (GHS) hazard classification:

Category	Oral LD <sub>50</sub> Limits
1	LD <sub>50</sub> ≤ 5 mg/kg
2	5 < LD <sub>50</sub> ≤ 50 mg/kg
3	50 < LD <sub>50</sub> ≤ 300 mg/kg
4	300 < LD <sub>50</sub> ≤ 2000 mg/kg
5	2000 < LD <sub>50</sub> ≤ 5000 mg/kg
Unclassified	LD <sub>50</sub> > 5000 mg/kg

## **Appendix J-6**

### **NHK NRU Predictions: RC Rat-Only Weight Regression**

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## NHK NRU Predictions: RC Rat-Only Weight Regression

RC Rat-Only Weight Regression:  $\log \text{LD}_{50} (\text{mg/kg}) = 0.372 \log \text{IC}_{50} (\text{ug/mL}) + 2.024$ 

Chemical <sup>a</sup>	Log Reference LD <sub>50</sub> (mg/kg) <sup>1</sup>	NHK Log IC <sub>50</sub> (ug/mL) <sup>2</sup>	Log Predicted LD <sub>50</sub> (mg/kg) <sup>3</sup>	Observed LD <sub>50</sub> (mg/kg) <sup>1</sup>	NHK IC <sub>50</sub> (ug/mL) <sup>2</sup>	Predicted LD <sub>50</sub> (mg/kg) <sup>3</sup>	Observed LD <sub>50</sub> -Predicted LD <sub>50</sub> (mg/kg)	Observed Toxicity Category <sup>4</sup> (mg/kg)	Predicted Toxicity Category <sup>4</sup> (mg/kg)
Acetaminophen	3.33	2.71	3.03	2162	518	1081	1081	2000-5000	300-2000
Acetonitrile	3.56	3.98	3.50	3595	9528	3193	402	2000-5000	2000-5000
Acetylsalicylic acid	3.18	2.78	3.06	1506	605	1145	361	300-2000	300-2000
Aminopterin	0.845	2.83	3.08	7.00	669	1189	-1182	5-50	300-2000
5-Aminosalicylic acid	3.54	1.67	2.64	3428	46.7	442	2986	2000-5000	300-2000
Arsenic III trioxide	1.40	0.721	2.29	25.1	5.26	196	-171	5-50	50-300
Boric acid	3.53	2.62	3.00	3426	421	1001	2425	2000-5000	300-2000
Busulfan	1.08	2.42	2.92	12.1	260	836	-824	5-50	300-2000
Cadmium II chloride	2.13	0.266	2.12	135	1.84	133	2.52	50-300	50-300
Chloramphenicol	3.54	2.54	2.97	3490	348	932	2558	2000-5000	300-2000
Citric acid	3.77	2.60	2.99	5929	400	981	4948	> 5000	300-2000
Cupric sulfate pentahydrate	2.68	2.29	2.88	475	197	754	-279	300-2000	300-2000
Cycloheximide	0.301	-1.13	1.60	2.00	0.073	40.0	-38.0	< 5	5-50
Dibutyl phthalate	3.95	1.46	2.57	8892	29	368	8524	> 5000	300-2000
Diethyl phthalate	3.97	2.08	2.80	9311	120	628	8683	> 5000	300-2000
Digoxin	1.45	-3.00	0.909	28.3	0.001	8.12	20.2	5-50	5-50
Dimethylformamide	3.72	3.89	3.47	5305	7760	2958	2347	> 5000	2000-5000
Diquat dibromide monohydrate	2.20	0.651	2.27	160	4.48	185	-24.6	50-300	50-300
Ethanol	4.05	4.00	3.51	11324	10018	3253	8071	> 5000	2000-5000
Ethylene glycol	3.85	4.62	3.74	7161	41852	5537	1624	> 5000	>5000
Gibberellic acid	3.78	3.46	3.31	6039	2856	2040	4000	> 5000	2000-5000
Glycerol	4.30	4.39	3.66	19770	24730	4553	15217	> 5000	2000-5000
Hexachlorophene	1.91	-1.54	1.45	82.0	0.03	28.3	53.7	50-300	5-50
Lactic acid	3.56	3.12	3.18	3635	1304	1524	2111	2000-5000	300-2000
Lithium I carbonate	2.77	2.67	3.02	590	468	1040	-450	300-2000	300-2000
Meprobamate	3.14	2.55	2.97	1387	357	941	446	300-2000	300-2000
Mercury II chloride	1.60	0.763	2.31	40.2	5.80	203	-163	5-50	50-300
Methanol	3.94	3.18	3.21	8710	1529	1616	7093	> 5000	300-2000
Phenol	2.74	1.88	2.72	548	75.0	527	21.0	300-2000	300-2000
Phenylthiourea	0.477	2.53	2.96	3.00	336	920	-917	< 5	300-2000
Potassium I chloride	3.45	3.35	3.27	2802	2237	1862	940	2000-5000	300-2000

## NHK NRU Predictions: RC Rat-Only Weight Regression

Chemical <sup>a</sup>	Log Reference LD <sub>50</sub> (mg/kg) <sup>1</sup>	NHK Log IC <sub>50</sub> (ug/mL) <sup>2</sup>	Log Predicted LD <sub>50</sub> (mg/kg) <sup>3</sup>	Observed LD <sub>50</sub> (mg/kg) <sup>1</sup>	NHK IC <sub>50</sub> (ug/mL) <sup>2</sup>	Predicted LD <sub>50</sub> (mg/kg) <sup>3</sup>	Observed LD <sub>50</sub> - Predicted LD <sub>50</sub> (mg/kg)	Observed Toxicity Category <sup>4</sup> (mg/kg)	Predicted Toxicity Category <sup>4</sup> (mg/kg)
2-Propanol	3.71	3.73	3.41	5105	5364	2579	2526	> 5000	2000-5000
Propranolol HCl	2.67	1.55	2.60	466	35.3	398	67.9	300-2000	300-2000
Sodium arsenite	1.64	-0.322	1.90	43.6	0.477	80.2	-36.6	5-50	50-300
Sodium chloride	3.61	3.30	3.25	4050	1997	1786	2264	2000-5000	300-2000
Sodium dichromate dihydrate	1.70	-0.142	1.97	50.5	0.72	93.6	-43.1	50-300	50-300
Sodium hypochlorite	4.01	3.18	3.21	10328	1502	1606	8722	> 5000	300-2000
Sodium I fluoride	2.10	1.70	2.66	127	49.8	452	-325	50-300	300-2000
Sodium oxalate	2.80	2.53	2.96	633	337	921	-288	300-2000	300-2000
Sodium selenate	0.477	1.01	2.40	3.00	10.2	251	-248	< 5	50-300
Thallium I sulfate	1.40	-0.819	1.72	25.0	0.152	52.4	-27.4	5-50	50-300
Trichloroacetic acid	3.72	2.62	3.00	5229	413	994	4235	> 5000	300-2000
1,1,1-Trichloroethane	4.08	3.91	3.48	12078	8122	3009	9069	> 5000	2000-5000
Triethylenemelamine	0.602	0.268	2.12	4.00	1.85	133	-129	< 5	50-300
Triphenyltin Hydroxide	2.52	-2.00	1.28	329	0.01	19.1	310	300-2000	5-50
Valproic acid	3.00	2.71	3.03	996	512	1076	-80.1	300-2000	300-2000
Xylene	3.67	2.67	3.02	4665	466	1039	3626	2000-5000	300-2000

<sup>a</sup>Three chemicals were excluded because no rat LD<sub>50</sub> was identified: epinephrine bitartrate, colchicine, and propylparaben. Carbon tetrachloride and methanol were excluded because an IC<sub>50</sub> value could not be determined. Twenty-one chemicals were excluded based on their mechanisms of action: amitriptyline HCl, atropine sulfate, caffeine, carbamazepine, chloral hydrate, dichlorvos, disulfoton, endosulfan, fenpropathrin, glutethimide, haloperidol, lindane, nicotine, paraquat, parathion, phenobarbital, physostigmine, potassium cyanide, procainamide HCl, strychnine, and verapamil HCl (see Section 6, Table 6-3).

<sup>1</sup>reference LD<sub>50</sub> values that were collected from the literature

<sup>2</sup>combined NHK IC<sub>50</sub> values from three laboratories

<sup>3</sup>LD<sub>50</sub> determined regression: log LD<sub>50</sub> (mg/kg) = 0.372 log IC<sub>50</sub> (ug/mL) + 2.024

<sup>4</sup>Globally Harmonized System (GHS) hazard classification:

Category	Oral LD <sub>50</sub> Limits
1	LD <sub>50</sub> ≤ 5 mg/kg
2	5 < LD <sub>50</sub> ≤ 50 mg/kg
3	50 < LD <sub>50</sub> ≤ 300 mg/kg
4	300 < LD <sub>50</sub> ≤ 2000 mg/kg
5	2000 < LD <sub>50</sub> ≤ 5000 mg/kg
Unclassified	LD <sub>50</sub> > 5000 mg/kg

## **Appendix J-7**

### **3T3 NRU Predictions: RC Rat-Only Weight Regression Excluding Chemicals with Specific Mechanisms of Toxicity**

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## 3T3 NRU Predictions: RC Rat-Only Regression Excluding Specific Mechanisms

RC Rat-Only Weight Regression Excluding Chemicals with Specific Mechanisms of Toxicity:  
 $\text{Log LD}_{50} \text{ (mg/kg)} = 0.357 \log \text{IC}_{50} \text{ (ug/mL)} + 2.194$

Chemical <sup>a</sup>	Log Observed LD <sub>50</sub> (mg/kg) <sup>1</sup>	3T3 Log IC <sub>50</sub> (ug/mL) <sup>2</sup>	Log Predicted LD <sub>50</sub> (mg/kg) <sup>3</sup>	Observed LD <sub>50</sub> (mg/kg) <sup>1</sup>	3T3 IC <sub>50</sub> (ug/mL) <sup>2</sup>	Predicted LD <sub>50</sub> (mg/kg) <sup>3</sup>	Observed LD <sub>50</sub> -Predicted LD <sub>50</sub> (mg/kg)	Observed Toxicity Category <sup>4</sup> (mg/kg)	Predicted Toxicity Category <sup>4</sup> (mg/kg)
Acetaminophen	3.33	1.68	2.79	2162	47.7	621	1541	2000-5000	300-2000
Acetonitrile	3.56	3.90	3.59	3595	7951	3859	-264	2000-5000	2000-5000
Acetylsalicylic acid	3.18	2.83	3.20	1506	676	1601	-95.0	300-2000	300-2000
Aminopterin	0.845	-2.20	1.41	7.00	0.006	25.5	-18.5	5-50	5-50
5-Aminosalicylic acid	3.54	3.22	3.34	3428	1667	2209	1219	2000-5000	2000-5000
Arsenic III trioxide	1.40	0.293	2.30	25.1	1.96	199	-174	5-50	50-300
Boric acid	3.53	3.27	3.36	3426	1850	2293	1133	2000-5000	2000-5000
Busulfan	1.08	1.89	2.87	12.1	77.7	739	-727	5-50	300-2000
Cadmium I chloride	2.13	-0.286	2.09	135	0.518	123.6	11.6	50-300	50-300
Chloramphenicol	3.54	2.11	2.95	3490	128	884	2606	2000-5000	300-2000
Citric acid	3.77	2.90	3.23	5929	796	1697	4232	> 5000	300-2000
Cupric sulfate pentahydrate	2.68	1.62	2.77	475	42.1	594	-119	300-2000	300-2000
Cycloheximide	0.301	-0.727	1.93	2.00	0.187	86.0	-84.0	< 5	50-300
Dibutyl phthalate	3.95	1.70	2.80	8892	49.7	630	8262	> 5000	300-2000
Diethyl phthalate	3.97	2.03	2.92	9311	107	830	8481	> 5000	300-2000
Digoxin	1.45	2.67	3.15	28.3	466	1401	-1373	5-50	300-2000
Dimethylformamide	3.72	3.72	3.52	5305	5224	3321	1984	> 5000	2000-5000
Diquat dibromide monohydrate	2.20	0.905	2.52	160	8.04	329	-169	50-300	50-300
Ethanol	4.05	3.81	3.56	11324	6523	3595	7729	> 5000	2000-5000
Ethylene glycol	3.85	4.39	3.76	7161	24317	5751	1410	> 5000	>5000
Gibberellic acid	3.78	3.89	3.58	6039	7810	3834	2205	> 5000	2000-5000
Glycerol	4.30	4.39	3.76	19770	24655	5780	13990	> 5000	>5000
Hexachlorophene	1.91	0.623	2.42	82.0	4.19	261	-179	50-300	50-300
Lactic acid	3.56	3.48	3.44	3635	3044	2739	896	2000-5000	2000-5000
Lithium I carbonate	2.77	2.75	3.18	590	562	1498	-908	300-2000	300-2000
Meprobamate	3.14	2.72	3.16	1387	519	1456	-69.6	300-2000	300-2000
Mercury II chloride	1.60	0.615	2.41	40.2	4.12	259	-219	5-50	50-300
Phenol	2.74	1.82	2.84	548	66.3	699	-151	300-2000	300-2000
Phenylthiourea	0.477	1.90	2.87	3.00	79.0	744	-741	< 5	300-2000
Potassium I chloride	3.45	3.55	3.46	2802	3551	2894	-91.9	2000-5000	2000-5000

## 3T3 NRU Predictions: RC Rat-Only Regression Excluding Specific Mechanisms

Chemical <sup>a</sup>	Log Observed LD <sub>50</sub> (mg/kg) <sup>1</sup>	3T3 Log IC <sub>50</sub> (ug/mL) <sup>2</sup>	Log Predicted LD <sub>50</sub> (mg/kg) <sup>3</sup>	Observed LD <sub>50</sub> (mg/kg) <sup>1</sup>	3T3 IC <sub>50</sub> (ug/mL) <sup>2</sup>	Predicted LD <sub>50</sub> (mg/kg) <sup>3</sup>	Observed LD <sub>50</sub> -Predicted LD <sub>50</sub> (mg/kg)	Observed Toxicity Category <sup>4</sup> (mg/kg)	Predicted Toxicity Category <sup>4</sup> (mg/kg)
2-Propanol	3.71	3.56	3.46	5105	3618	2913	2192	> 5000	2000-5000
Propranolol HCl	2.67	1.14	2.60	466	13.9	399	66.5	300-2000	50-300
Sodium arsenite	1.64	-0.120	2.15	43.6	0.759	142	-98.0	5-50	50-300
Sodium chloride	3.61	3.67	3.51	4050	4730	3206	844	2000-5000	2000-5000
Sodium dichromate dihydrate	1.70	-0.232	2.11	50.5	0.587	129	-78.7	50-300	50-300
Sodium hypochlorite	4.01	3.04	3.28	10328	1103	1906	8422	> 5000	300-2000
Sodium 1 fluoride	2.10	1.89	2.87	127	78.0	741	-614	50-300	300-2000
Sodium oxalate	2.80	1.58	2.76	633	37.7	571	61.6	300-2000	300-2000
Sodium selenate	0.477	1.46	2.72	3.00	29.0	520	-517	< 5	300-2000
Thallium I sulfate	1.40	0.759	2.46	25.0	5.74	292	-267	5-50	50-300
Trichloroacetic acid	3.72	2.96	3.25	5229	902	1774	3455	> 5000	300-2000
1,1,1-Trichloroethane	4.08	4.24	3.71	12078	17248	5088	6990	> 5000	>5000
Triethylenemelamine	0.602	-0.565	1.99	4.00	0.272	98.2	-94.2	< 5	50-300
Triphenyltin hydroxide	2.52	-1.76	1.56	329	0.017	36.7	292	300-2000	5-50
Valproic acid	3.00	2.96	3.25	996	916	1784	-788	300-2000	300-2000
Xylene	3.67	2.86	3.21	4665	721	1638	3027	2000-5000	300-2000

<sup>a</sup>Three chemicals were excluded because no rat LD<sub>50</sub> was identified: epinephrine bitartrate, colchicine, and propylparaben. Carbon tetrachloride and methanol were excluded because IC<sub>50</sub> values could not be determined. Twenty-one chemicals were excluded based on their mechanisms of action: amitriptyline HCl, atropine sulfate, caffeine, carbamazepine, chloral hydrate, dichlorvos, disulfoton, endosulfan, fenpropathrin, glutethimide, haloperidol, lindane, nicotine, paraquat, parathion, phenobarbital, physostigmine, potassium cyanide, procainamide HCl, strychnine, and verapamil HCl. (see **Section 6, Table 6-3**)

<sup>2</sup> combined 3T3 IC<sub>50</sub> values from three laboratories

<sup>3</sup>LD<sub>50</sub> determined using RC regression: Predicted LD<sub>50</sub> mg/kg (RC rat [weight units]) = 0.357 log IC<sub>50</sub> ug/mL + 2.194; used 3T3 IC<sub>50</sub> and reference LD<sub>50</sub> values

<sup>4</sup>Globally Harmonized System (GHS) hazard classification

Category	Oral LD <sub>50</sub> Limits
1	LD <sub>50</sub> ≤ 5 mg/kg
2	5 < LD <sub>50</sub> ≤ 50 mg/kg
3	50 < LD <sub>50</sub> ≤ 300 mg/kg
4	300 < LD <sub>50</sub> ≤ 2000 mg/kg
5	2000 < LD <sub>50</sub> ≤ 5000 mg/kg
Unclassified	LD <sub>50</sub> > 5000 mg/kg

## **Appendix J-8**

### **NHK NRU Predictions: RC Rat-Only Weight Regression Excluding Chemicals with Specific Mechanisms of Toxicity**

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## NHK NRU Predictions: RC Rat-Only Regression Excluding Specific Mechanisms

RC Rat-Only Weight Regression Excluding Chemicals with Specific Mechanisms of Toxicity:  
 $\text{Log LD}_{50} (\text{mg/kg}) = 0.357 \text{ log IC}_{50} (\text{ug/mL}) + 2.194$

Chemical <sup>a</sup>	Log Observed LD <sub>50</sub> (mg/kg) <sup>1</sup>	NHK Log IC <sub>50</sub> (ug/mL) <sup>2</sup>	Log Predicted LD <sub>50</sub> (mg/kg) <sup>3</sup>	Observed LD <sub>50</sub> (mg/kg) <sup>1</sup>	NHK IC <sub>50</sub> (ug/mL) <sup>2</sup>	Predicted LD <sub>50</sub> (mg/kg) <sup>3</sup>	Observed LD <sub>50</sub> - Predicted LD <sub>50</sub> (mg/kg)	Observed Toxicity Category <sup>4</sup> (mg/kg)	Predicted Toxicity Category <sup>4</sup> (mg/kg)
Acetaminophen	3.33	2.71	3.16	2162	518	1456	706	2000-5000	300-2000
Acetonitrile	3.56	3.98	3.61	3595	9528	4116	-521	2000-5000	2000-5000
Acetylsalicylic acid	3.18	2.78	3.19	1506	605	1539	-32.9	300-2000	300-2000
Aminopterin	0.845	2.83	3.20	7.00	669	1595	-1588	5-50	300-2000
5-Aminosalicylic acid	3.54	1.67	2.79	3428	46.7	617	2811	2000-5000	300-2000
Arsenic III trioxide	1.40	0.721	2.45	25.1	5.26	283	-258	5-50	50-300
Boric acid	3.53	2.62	3.13	3426	421	1352	2074	2000-5000	300-2000
Busulfan	1.08	2.42	3.06	12.1	260	1138	-1126	5-50	300-2000
Cadmium II chloride	2.13	0.266	2.29	135	1.84	194	-59.3	50-300	50-300
Chloramphenicol	3.54	2.54	3.10	3490	348	1263	2227	2000-5000	300-2000
Citric acid	3.77	2.60	3.12	5929	400	1327	4602	> 5000	300-2000
Cupric sulfate pentahydrate	2.68	2.29	3.01	475	197	1030	-555	300-2000	300-2000
Cycloheximide	0.301	-1.13	1.79	2.00	0.073	61.5	-59.5	< 5	50-300
Dibutyl phthalate	3.95	1.46	2.71	8892	28.7	518	8374	> 5000	300-2000
Diethyl phthalate	3.97	2.08	2.94	9311	120	865	8446	> 5000	300-2000
Digoxin	1.45	-3.00	1.12	28.3	0.001	13.3	15.0	5-50	5-50
Dimethylformamide	3.72	3.89	3.58	5305	7760	3826	1479	> 5000	2000-5000
Diquat dibromide monohydrate	2.20	0.651	2.43	160	4.48	267	-107	50-300	50-300
Ethanol	4.05	4.00	3.62	11324	10018	4191	7133	> 5000	2000-5000
Ethylene glycol	3.85	4.62	3.84	7161	41852	6982	179	> 5000	> 5000
Gibberellic acid	3.78	3.46	3.43	6039	2856	2677	3362	> 5000	2000-5000
Glycerol	4.30	4.39	3.76	19770	24730	5786	13984	> 5000	> 5000
Hexachlorophene	1.91	-1.54	1.64	82.0	0.029	44.1	37.9	50-300	5-50
Lactic acid	3.56	3.12	3.31	3635	1304	2024	1611	2000-5000	2000-5000
Lithium I carbonate	2.77	2.67	3.15	590	468	1403	-813	300-2000	300-2000
Meprobamate	3.14	2.55	3.11	1387	357	1274	113	300-2000	300-2000
Mercury II chloride	1.60	0.763	2.47	40.2	5.80	293	-253	5-50	50-300
Methanol	3.94	3.18	3.33	8710	1529	2142	6568	> 5000	2000-5000
Phenol	2.74	1.88	2.86	548	75.0	730	-183	300-2000	300-2000
Phenylthiourea	0.477	2.53	3.10	3.00	336	1248	-1245	< 5	300-2000
Potassium I chloride	3.45	3.35	3.39	2802	2237	2454	348	2000-5000	2000-5000

## NHK NRU Predictions: RC Rat-Only Regression Excluding Specific Mechanisms

Chemical <sup>a</sup>	Log Observed LD <sub>50</sub> (mg/kg) <sup>1</sup>	NHK Log IC <sub>50</sub> (ug/mL) <sup>2</sup>	Log Predicted LD <sub>50</sub> (mg/kg) <sup>3</sup>	Observed LD <sub>50</sub> (mg/kg) <sup>1</sup>	NHK IC <sub>50</sub> (ug/mL) <sup>2</sup>	Predicted LD <sub>50</sub> (mg/kg) <sup>3</sup>	Observed LD <sub>50</sub> - Predicted LD <sub>50</sub> (mg/kg)	Observed Toxicity Category <sup>4</sup> (mg/kg)	Predicted Toxicity Category <sup>4</sup> (mg/kg)
2-Propanol	3.71	3.73	3.53	5105	5364	3353	1752	> 5000	2000-5000
Propranolol HCl	2.67	1.55	2.75	466	35.3	558	-92.1	300-2000	300-2000
Sodium arsenite	1.64	-0.322	2.08	43.6	0.477	120	-76.4	5-50	50-300
Sodium chloride	3.61	3.30	3.37	4050	1997	2356	1694	2000-5000	2000-5000
Sodium dichromate dihydrate	1.70	-0.142	2.14	50.5	0.721	139	-88.6	50-300	50-300
Sodium hypochlorite	4.01	3.18	3.33	10328	1502	2129	8199	> 5000	2000-5000
Sodium I fluoride	2.10	1.70	2.80	127	49.8	631	-504	50-300	300-2000
Sodium oxalate	2.80	2.53	3.10	633	337	1248	-615	300-2000	300-2000
Sodium selenate	0.477	1.01	2.55	3.00	10.2	358	-355	< 5	300-2000
Thallium I sulfate	1.40	-0.82	1.90	25.0	0.152	79.7	-54.7	5-50	50-300
Trichloroacetic acid	3.72	2.62	3.13	5229	413	1343	3886	> 5000	300-2000
1,1,1-Trichloroethane	4.08	3.91	3.59	12078	8122	3888	8190	> 5000	2000-5000
Triethylenemelamine	0.602	0.27	2.29	4.00	1.85	195	-191	< 5	50-300
Triphenyltin hydroxide	2.52	-2.00	1.48	329	0.010	30.3	299	300-2000	5-50
Valproic acid	3.00	2.71	3.16	996	512	1450	-454	300-2000	300-2000
Xylene	3.67	2.67	3.15	4665	466	1401	3264	2000-5000	300-2000

<sup>a</sup>Three chemicals were excluded because no rat LD<sub>50</sub> was identified: eninenhrine bitartrate, colchicine, and propylparaben. Carbon tetrachloride excluded because an IC<sub>50</sub> value could not be determined. Twenty-one chemicals were excluded based on their mechanisms of action: amitriptyline HCl, atropine sulfate, caffeine, carbamazepine, chloral hydrate, dichlorvos, disulfoton, endosulfan, fenpropathrin, glutethimide, haloperidol, lindane, nicotine, paraquat, parathion, phenobarbital, physostigmine, potassium cyanide, procainamide HCl, strychnine, and verapamil HCl. (see Section 6, Table 6-3)

<sup>1</sup>reference LD<sub>50</sub> values that were collected from the literature

<sup>2</sup>combined NHK IC<sub>50</sub> values from three laboratories

<sup>3</sup>LD<sub>50</sub> determined using RC regression: Predicted LD<sub>50</sub> mg/kg (RC rat [weight units]) = 0.357 log IC<sub>50</sub> ug/mL + 2.194; used NHK IC<sub>50</sub> and reference LD<sub>50</sub> values

<sup>4</sup>Globally Harmonized System (GHS) hazard classification:

Category	Oral LD <sub>50</sub> Limits
1	LD <sub>50</sub> ≤ 5 mg/kg
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4	300 < LD <sub>50</sub> ≤ 2000 mg/kg
5	2000 < LD <sub>50</sub> ≤ 5000 mg/kg
Unclassified	LD <sub>50</sub> > 5000 mg/kg