Supplemental Material

Expanding the toolbox: hazard-screening methods and tools for identifying safer chemicals in green product design

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Table S1. Chemical Test Set 1

Chemical Name	CAS RN	MW (g/mol)	Water Solubility[a] mg/L	T °C	LogK$_{OW}$[a]	Vapor Pressure[a] mmHg	T °C	Similarity Score ChemMine	Similarity Score ToxMatch	Structural Alert ToxTree	Structural Alert Derek Nexus™	Structural Alert Match Target?	Animal Test Data S/NS	Animal Test Data Source
4-Phenylenediamine	106-50-3	108.14	**3.70E+04**	23	**-0.3**	5.00E-03	25	N/A	N/A	Yes	Yes	-	S	NTP 2013
4-Chloroaniline	106-47-8	127.57	**3900**	25	**1.83**	**0.027**	26	0.6	0.448	No	Yes	No	NS	NTP 2013
1,3-phenylenediamine	108-45-2	108.14	**2.38E+05**	20	**-0.33**	**2.09E-03**	25	0.51314	0.812	Yes	Yes	No	S	NTP 2013
Toluene 2,4 diamine	95-80-7	122.17	7.48E+04	25	**0.14**	**1.70E-04**	25	0.454545	0.52	Yes	Yes	No	S	NTP 2013
2,5-Diaminotoluene sulfate[b]	615-50-9	220.25	NA	25	NA	NA	25	0.45098	0.467	Yes	Yes	Yes	S	NTP 2013
Aniline	62-53-3	93.13	**3.60E-04**	25	**0.9**	**0.49**	25	0.441176	0.929	No	Yes	No	S	NTP 2013
4-Aminobenzoic acid	150-13-0	137.14	**6110**	30	**0.83**	2.78E-04	25	0.403846	0.351	No	Yes	No	NS	NTP 2013
2-Nitro-1,4-phenylendiamine	5307-14-2	153.14	2.59E+04	25	**0.53**	5.60E-05	25	0.383333	0.35	Yes	Yes	Yes	S	NTP 2013
1,4-dichlorobenzene	106-46-7	147.00	**81.3**	25	**3.44**	**1.74**	25	0.365854	0.214	No	No	No	NS	ECHA 2016
2-Aminophenol	95-55-6	109.13	**2.00E+04**	20	**0.62**	9.55E-03	25	0.365854	0.684	Yes	Yes	Yes	S	NTP 2013
3-Aminophenol	591-27-5	109.13	**2.70E+04**	25	**0.21**	9.55E-03	25	0.365854	0.684	Yes	Yes	No	S	NTP 2013
Benzoquinone	106-51-4	108.10	**1.11E+04**	18	**0.2**	**9.00E-02**	25	0.365854	0.1	Yes	Yes	No	S	NTP 2013
Hydroquinone (p-benzenediol)	123-31-9	110.11	**7.20E+04**	25	**0.59**	**2.40E-05**	25	0.365854	0.556	Yes	Yes	No	S	NTP 2013
2-Amino-5-methylphenol	2835-98-5	123.15	1.03E+04	25	1.14	0.00308	25	0.361702	0.481	Yes	Yes	Yes	S	Natsch et al. 2015
3,4-Dichloroaniline hydrochloride	95-76-1	162.02	**92**	20	**2.69**	**0.00632**	25	0.361702	0.371	No	Yes	No	S	NTP 2013
4-Amino-3-methylphenol	2835-99-6	123.15	2.06E+04	25	0.79	0.00308	25	0.361702	0.519	Yes	Yes	Yes	S	NTP 2013
5-Amino-2-methylphenol	2835-95-2	123.15	2.06E+04	25	0.79	0.00308	25	0.361702	0.464	Yes	Yes	No	S	NTP 2013
4-Aminobenzenesulfonic acid	121-57-3	173.19	**1.08E+04**	20	**-2.16**	**2.02E-07**	25	0.33871	0.368	No	Equivocal[c]	No	NS	Natsch et al. 2015
4-Nitrobenzene-1,2-diamine	99-56-9	153.14	1.30E+04	25	**0.88**	1.09E-04	25	0.31746	0.359	Yes	Yes	Yes	S	Natsch et al. 2015
4-Hydroxybenzaldehyde	123-08-0	122.12	**8450**	25	**1.35**	**1.13E-04**	25	0.306122	0.312	Yes	Equivocal[c]	No	NS	Natsch et al. 2015
Benzocaine	94-09-7	165.20	**1.31E+03**	30	**1.86**	2.58E-04	25	0.287671	0.245	No	Yes	No	S	NTP 2013
4-Hydroxybenzoic acid	99-96-7	138.12	**5000**	25	**1.58**	**1.92E-07**	25	0.258621	0.25	No	Equivocal[c]	No	NS	NTP 2013
4-Amino-3-nitrophenol	610-81-1	154.12	7045	25	1.19	3.52E-05	25	0.257576	0.326	Yes	Yes	Yes	S	NTP 2013
Chlorobenzene	108-90-7	112.56	**498**	25	**2.84**	**12**	25	0.25641	0.222	No	No	No	NS	NTP 2013
Phenol	108-95-2	94.11	**8.28E+04**	25	**1.46**	**0.35**	25	0.25641	0.588	No	No	No	NS	Natsch et al. 2015
Methylenedianiline	101-77-9	198.27	**1.00E+03**	25	**1.59**	2.97	25	0.254717	0.342	No	Yes	No	S	ECHA 2016
Benzaldehyde	100-52-7	106.12	**6570**	25	**1.48**	**0.127**	25	0.244444	0.259	Yes	No	No	S	Natsch et al. 2012
Catechol (o-benzenediol)	120-80-9	110.11	**4.61E+05**	25	**0.88**	**3.66E-03**	25	0.244444	0.526	Yes	Yes	No	S	ECHA 2016
Resorcinol (m-benzenediol)	108-46-3	110.11	**7.17E+05**	25	**0.8**	**4.89E-04**	25	0.244444	0.526	Yes	Yes	No	S	NTP 2013
Xylene; 3-xylene	1330-20-7	107.17	**106**	25	**3.16**	**7.99**	25	0.244444	0.273	No	No	No	NS	Natsch et al. 2015
Benzoic acid	65-85-0	122.12	**3400**	25	**1.87**	**7.00E-04**	25	0.230769	0.235	No	No	No	NS	NTP 2013
2-Fluoro-5-nitroaniline	369-36-8	156.12	2662	25	1.67	0.00352	25	0.220588	0.289	No	Yes	No	NS	NTP 2013
N,N-dimethyl-4-nitrosoaniline	138-89-6	150.18	1370	25	2.04	0.406	25	0.220588	0.467	Yes	No	No	S	Natsch et al. 2015
Benzyl alcohol	100-51-6	108.14	**4.29E+04**	25	**1.1**	**0.094**	25	0.217391	0.308	No	No	No	NS	Natsch et al. 2015
n-Methylaniline	100-61-8	107.16	**5620**	25	**1.66**	**0.453**	25	0.217391	0.65	No	Yes	No	NS	ECHA 2016
3-Hydroxy-4-methoxybenzaldehyde	621-59-0	152.15	1.10E+04	25	**0.97**	1.03E-03	25	0.202899	0.208	Yes	No	No	NS	NTP 2013
2-Amino-di-phenylamine	534-85-0	184.24	492.6	25	2.37	0.000295	25	0.20202	0.351	Yes	Yes	Yes	S	NTP 2013
(S)-(-)-1-Phenylpropylamine	3789-59-1	135.21	5492.3	25	1.98	0.201	25	0.196721	0.205	No	No	No	NS	NTP 2013
Creosol	93-51-6	138.17	2090	25	1.88	0.024	25	0.196721	0.263	Yes	Yes	No	S	NTP 2013
tert-Butyl-3-aminobenzoate	92146-82-2	193.24	249	25	2.67	0.000839	25	0.19	0.228	No	Yes	No	NS	NTP 2013
Dimethylaniline	121-69-7	121.18	**1.45E+03**	25	**2.31**	**0.7**	25	0.185185	0.65	No	No	No	S	NLM 2015
N-Ethyl-m-toluidine	102-27-2	135.21	470	25	2.66	0.13	25	0.177419	0.342	No	Yes	No	NS	ACC 2001
Salicylic acid	69-72-7	138.12	**2240**	25	**2.26**	**8.20E-05**	25	0.177419	0.238	No	Yes	No	NS	Natsch et al. 2015
2,4-Dichloronitrobenzene	611-06-3	192.00	68.9	25	**3.07**	0.014	25	0.169014	0.213	Yes	Yes	No	S	Natsch et al. 2015
Benzene	71-43-2	78.11	**1790**	25	**2.13**	**94.8**	25	0.162162	0.429	No	No	No	NS	ECHA 2016
4-Methylaminophenol sulfate[b]	55-55-0	344.39	**5.00E+04**	NA	0.79	NA	25	0.157895	0.467	Yes	Yes	Yes	S	NTP 2013
3-Propoxybenzoic acid	190965-42-5	180.20	170.3	25	2.94	0.000235	25	0.152174	0.139	No	No	No	NS	NTP 2013
2-Methyl-5-hydroxyethylaminophenol	55302-96-0	167.21	1.55E+05	25	0.37	7.19E-06	25	0.146341	0.236	Yes	No	No	S	NTP 2013
N,N-Diethylaniline	91-66-7	149.24	**140**	25	**3.31**	**0.136**	25	0.136986	0.464	No	No	No	NS	ECHA 2016
3,4-dinitrophenol	577-71-9	184.11	1.45E+04	25	1.73	1.20E-05	25	0.12766	0.298	No	No	No	S	NTP 2013
2,6-Dimethoxyphenol	91-10-1	154.16	**1.72E+04**	13	**1.15**	6.17E-03	25	0.121622	0.303	Yes	Yes	No	NS	Natsch et al. 2015
2,6-dimethylbenzoic acid	632-46-2	150.18	982	25	**2.21**	1.54E-03	25	0.121622	0.19	No	No	No	NS	NTP 2013
2-Chloro-6-nitrotoluene	83-42-1	171.58	56.6	25	**3.09**	0.011	25	0.121622	0.191	No	No	No	NS	NTP 2013
2-Amino-6-chloro-4-nitrophenol	6358-09-4	188.57	2470	25	**1.53**	6.69E-06	25	0.119048	0.203	Yes	Yes	Yes	S	NTP 2013
N-isopropyl-N'-phenyl-p-phenylenediamine	101-72-4	226.32	54.6	25	3.28	7.11E-05	25	0.100671	0.311	Yes	Yes	Yes	S	NTP 2013
N,N-dibutylaniline	613-29-6	205.34	5.70E+00	25	5.12	7.10E-03	25	0.0813008	0.302	No	No	No	S	NTP 2013

Notes:

CAS RN = Chemical Abstracts Service Registry Number; MW = Molecular weight; NA = Not available; NS = Non-sensitizer; S = Sensitizer; T = Temperature; TS = Test set.

Grey shading represents exclusion from the refined test set based on physicochemical property data, Tanimoto score, and/or structural alert(s).

Physicochemical properties reported by ChemID (NLM 2016) and/or Epi Suite™ (US EPA 2012).

(a) Experimental values are shown in bold text, whereas estimated values are shown in normal text.

(b) Sulfate salts were not excluded based on their total molecular weights. Rather, the molecular weights of the cation species were considered.

(c) Equivocal structural alerts were treated as neither a positive nor a negative result.

Table S2. Chemical Test Set 2

Chemical Name	CAS RN	MW (g/mol)	Water Solubility[a] mg/L	T °C	$LogK_{OW}$[a]	Vapor Pressure[a] mmHg	T °C	Similarity Score ChemMine	ToxMatch	Structural Alerts ToxTree	Derek Nexus™	Match Target?	Animal Test Data S/NS	Source
Hydroxyethylacrylate	818-61-1	116.12	**1000000**	25	**-0.21**	**0.0523**	25	N/A	N/A	Yes	Yes	-	S	NTP 2013
Hydroxylethylmethacrylate	868-77-9	130.14	**100000**	25	**0.47**	**0.126**	25	0.488372	0.793	Yes	Yes	Yes	S	ECHA 2016
Butylacrylate	141-32-2	128.17	**2000**	23	**2.36**	**5.45**	25	0.488372	0.543	Yes	Yes	Yes	S	NTP 2013
2-Hydroxypropylacrylate	999-61-1	130.14	**1000000**	25	**0.35**	0.174	25	0.488372	0.793	Yes	Yes	Yes	S	ECHA 2016
Ethyl acrylate	140-88-5	100.12	**15000**	25	**1.32**	**38.6**	25	0.441176	0.826	Yes	Yes	Yes	S	NTP 2013
Methyl acrylate	96-33-3	86.09	**49400**	25	**0.8**	**86.6**	25	0.30303	0.696	Yes	Yes	Yes	S	NTP 2013
Hydroxypropylmethacrylate	923-26-2	144.17	108000	25	**0.97**	0.0724	25	0.280702	0.742	Yes	Yes	Yes	S	NICNAS 2017
Ethylmethacrylate	97-63-2	114.14	**5400**	25	**1.94**	**20.6**	25	0.244444	0.679	Yes	Yes	Yes	S	ECHA 2016
1,4-Butanediol vinyl ether	17832-28-9	116.16	160000	25	0.43	0.248	25	0.217391	0.216	No	Equivocal[b]	No	NS	ECHA 2016
1,4-Butanediol diacrylate	1070-70-8	198.22	729	25	2.1	0.11	25	0.214286	0.422	Yes	Yes	Yes	S	Golla et al. 2009
2-Methoxyethanol	109-86-4	76.1	**1000000**	25	**-0.77**	**9.5**	25	0.1875	0.391	No	No	No	NS	ECHA 2016
Acrylic acid	79-10-7	72.06	**1000000**	25	**0.35**	**3.97**	25	0.1875	0.522	Yes	No	No	NS	ECHA 2016
Methyl vinyl ketone	78-94-4	70.09	10977	25	0.41	91.3	25	0.1875	0.32	Yes	Yes	Yes	S	DFG 1998
2-Ethylhexyl acrylate	103-11-7	184.28	**100**	25	4.09	**0.178**	25	0.177778	0.404	Yes	Yes	Yes	S	NTP 2013
2-Ethoxyethanol	110-80-5	90.12	**1000000**	25	**-0.32**	**5.31**	25	0.162162	0.478	No	No	No	NS	ECHA 2016
4-Hydroxybutan-2-one	590-90-9	88.11	1000000	25	-1.21	0.857	25	0.162162	0.241	No	No	No	S	ECHA 2016
Ethyleneglycol dimethacrylate	97-90-5	198.22	1969	25	2.21	84.7	25	0.144231	0.561	Yes	Yes	Yes	S	NTP 2013
Methyl methacrylate	80-62-6	100.12	**15000**	25	**1.38**	**38.5**	25	0.139535	0.593	Yes	Yes	Yes	S	NTP 2013
2-Propoxyethanol	2807-30-9	104.15	470000	25	0.08	**3.12**	25	0.139535	0.393	No	No	No	NS	ECHA 2016
Methyl crotonate	623-43-8	100.12	28427	25	1.14	17.1	25	0.139535	0.593	Yes	Yes	Yes	S	SCCNFP 2000
2-Butoxyethanol	111-76-2	118.18	**1000000**	20	**0.83**	**0.88**	25	0.12	0.333	No	No	No	NS	ECHA 2016
2-Heptanone	110-43-0	114.19	**4300**	25	**1.98**	**3.86**	25	0.12	0.156	No	No	No	NS	ECHA 2016
2,2-Dimethyl 3-methyl-3-butenyl propanoate	104468-21-5	170.25	188.85	25	3.62	0.805	25	0.119048	0.366	No	No	No	NS	ECHA 2016
Vinyl acetate	108-05-4	86.09	**20000**	20	**0.73**	**90.2**	20	0.102564	0.444	Yes	Equivocal[b]	No	NS	ECHA 2016
Tetraethylene_Glycol_Diacrylate	17831-71-9	302.32	52707	25	**1.26**	0.000308	25	0.0967742	0.657	Yes	Yes	Yes	NS	Golla et al. 2009
Methacrylic acid	79-41-4	86.09	**89000**	25	**0.93**	**0.99**	25	0.075	0.462	Yes	No	No	NS	ECHA 2016
Trimethylolpropanetriacrylate	15625-89-5	296.32	74.3	25	2.86	0.000563	25	0.0672646	0.422	Yes	Yes	Yes	S	NTP 2013
Isopropenyl acetate	108-22-5	100.12	21850	25	1.28	42.6	25	0.0652174	0.556	Yes	No	No	NS	ECHA 2016
Crotonaldehyde	4170-30-3	70.09	**181000**	20	0.6	**30**	20	0.027027	0.32	Yes	Yes	Yes	NS	ECHA 2016

Notes:

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Grey shading represents exclusion from the refined test set based on physicochemical property data, Tanimoto score, and/or structural alert(s).

Physicochemical properties reported by ChemID (NLM 2016) and/or Epi Suite™ (US EPA 2012).

(a) Experimental values are shown in bold text, whereas estimated values are shown in normal text.

(b) Equivocal structural alerts were treated as neither a positive nor a negative result.

Table S3. Chemical Test Set 3

Chemical Name	CAS RN	MW (g/mol)	Water Solubility[a]		$LogK_{OW}$[a]	Vapor Pressure[a]		Similarity Score		Structural Alert			Animal Test Data	
			mg/L	T °C		mmHg	T °C	ChemMine	ToxMatch	ToxTree	Derek Nexus™	Match Target	S/NS	Source
Methylisothiazolone	2682-20-4	115.2	960000	25	-0.83	0.031	25	N/A	N/A	Yes	Yes	-	S	NTP 2013
5-Chloro-2-methyl-4-isothiazolin-3-one	26172-55-4	149.6	320000	25	-0.34	0.0054	25	0.441176	0.613	Yes	Yes	Yes	S	NTP 2013
4,5-Dichloro-2-methyl-4-isothiazolin-3-one	26542-23-4	184	100000	25	0.15	0.00101	25	0.212766	0.245	Yes	Yes	Yes	S	Golla et al. 2009
N,N-Dimethylacetamide	127-19-5	87.1	**1000000**	25	**-0.77**	**2**	25	0.2	0.289	No	No	No	NS	ECHA 2016
2,3,5,6-Tetrahydro-2-methyl-2H-cyclopenta(d)-1,2-thiazol-3-one	82633-79-2	155.2	130000	25	0.64	0.000662	25	0.178571	0.236	Yes	Yes	Yes	S	NTP 2013
Methylpyrrolidone	872-50-4	99.1	**1000000**	25	**-0.38**	**0.345**	25	0.166667	0.216	No	No	No	NS	ECHA 2016
Octhilinone	26530-20-1	213.3	**500**	25	**2.45**	**0.0000368**	25	0.154639	0.447	Yes	Yes	Yes	S	Health Canada 2015
2-Methylimidazole	693-98-1	82.1	80900	25	**0.24**	0.015	25	0.125	0.143	No	No	No	NS	ECHA 2016
Furfural	98-01-1	96.1	**77000**	25	**0.41**	**2.21**	25	0.105263	0.077	Yes	No	No	NS	ECHA 2016

Notes:

CAS RN = Chemical Abstracts Service Registry Number; MW = Molecular weight; NA = Not available; NS = Non-sensitizer; S = Sensitizer; T = Temperature; TS = Test set.

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Physicochemical properties reported by ChemID (NLM 2016) and/or Epi Suite™ (US EPA 2012).

(a) Experimental values are shown in bold text, whereas estimated values are shown in normal text.

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