

Supplemental material: Derivation of internal dose-based thresholds of toxicological concern for occupational inhalation exposure to systemically-acting organic chemical vapors

PBPK model predictions of the three measures of internal dose, for each of the 276 studied chemicals, obtained in this study: daily rate of the amount of parent chemical metabolized (RMET₂₄), 24-h area under the venous blood concentration versus time curve (AUC₂₄) and maximum venous blood concentration at the end of an 8-h workshift. (CMAX₈).

Name	LogRMET24mmol/d	LogAUC24mmol/L.h	LogCMAX8mmol/L
(1-methylethenyl)-Benzene	0.43	-1.59	-2.56
(2-Methoxymethylethoxy)propanol (DPGME)	0.88	-1.24	-2.42
1-Bromopropane	-2.14	-3.87	-4.80
1-Butene	0.01	-1.19	-2.10
1-Chloro-1-nitropropane	-0.55	-1.40	-2.44
1-Chloro-2-propanol	-0.81	-2.15	-3.22
1-Hexene	0.09	-1.56	-2.48
1-Methylnaphthalene	-0.85	-2.42	-3.42
1-Nitropropane	0.44	0.21	-0.80
1,1-Dichloroethane	0.75	-0.69	-1.62
1,1,1,2-Tetrachloro-2,2-difluoroethane	0.66	-1.36	-2.28
1,1,2-Trichloro-1,2,2-trifluoroethane	0.99	-1.02	-1.93
1,1,2-Trichloroethane	0.40	-1.62	-2.57
1,1,2,2-Tetrabromoethane	-1.57	-3.60	-4.63
1,1,2,2-Tetrachloro-1,2-difluoroethane	0.26	-1.77	-2.69
1,1,2,2-Tetrachloroethane	-0.54	-2.52	-3.48
1,2-dichloroethylene	1.30	-0.71	-1.64
1,2-Dichloroethylene (cis-)	1.30	-0.71	-1.64
1,2-Dichloroethylene (trans-)	1.30	-0.71	-1.64
1,3-Dichloropropene	-0.82	-2.18	-3.14
1,3-Dioxolane	0.45	-0.66	-1.70
1,3,5-Triglycidyl-s-triazinetriene	-3.95	-8.34	-9.64
1,4-Dioxane	0.49	-0.98	-2.04
2-Aminopyridine	-1.33	-3.40	-4.56
2-Butene	-0.08	-1.11	-2.01
2-Butene (cis-)	-0.08	-1.11	-2.01
2-Butene (trans-)	-0.08	-1.11	-2.01
2-Butoxyethyl acetate (EGBEA)	0.53	-0.74	-1.70
2-Chloro-1-propanol	-0.81	-1.99	-3.05
2-Chloropropionic acid	-1.78	-3.56	-4.56
2-Diethylaminoethanol	-0.94	-3.15	-4.33
2-Ethoxyethanol (EGEE)	-0.08	-1.42	-2.43
2-Ethoxyethyl acetate (EGEEA)	-0.08	-1.47	-2.43
2-Ethylhexanoic acid	-0.90	-2.86	-3.83
2-Isopropoxyethanol	0.61	-0.47	-1.49
2-Methoxyethanol (EGME)	-1.78	-3.25	-4.26
2-Methoxyethyl acetate (EGMEA)	-1.81	-3.81	-4.88
2-Methylbutane	0.36	-0.50	-1.41
2-Methylhexane	0.61	-0.51	-1.42
2-Methylnaphthalene	-0.85	-2.40	-3.41
2-Methylpentane	0.56	-0.61	-1.51
2-Nitropropane	0.00	-0.28	-1.27
2-Oxetanone	-1.08	-1.09	-1.99

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2-Propanol	1.48	0.02	-1.04
2,2-Dimethylbutane	0.47	-0.77	-1.68
2,2-Dimethylpentane	0.61	-0.69	-1.60
2,3-Dimethylbutane	0.56	-0.61	-1.51
2,3-Dimethylpentane	0.81	-0.49	-1.40
2,4-D	-0.76	-1.15	-2.20
2,4-Dimethylpentane	0.76	-0.66	-1.58
2,4-Pentanedione	0.56	-0.40	-1.50
2,4,5-T	-0.87	-2.41	-3.42
2,4,6-Trinitrotoluene	-2.74	-2.52	-3.48
3-Methylhexane	0.91	-0.52	-1.44
3-Methylpentane	0.58	-0.55	-1.46
3,5-Dinitro-o-toluamide	-1.77	-3.01	-4.07
4-Methoxyphenol	-0.86	-1.78	-2.89
4-Vinyl cyclohexene	-1.82	-3.84	-4.78
4,4'-Methylene dianiline	-1.84	-3.86	-4.82
5-Nitro-o-toluidine	-1.62	-2.69	-3.76
Acetic acid	0.06	-1.98	-3.14
Acetone	1.54	0.08	-0.96
Acetophenone	0.18	-0.17	-1.22
Acrylamide	-2.79	-4.62	-5.67
Acrylonitrile	-0.47	-1.15	-2.09
Adipic acid	-0.87	-2.12	-3.16
Alachlor	-1.89	-3.90	-4.86
Aldrin	-3.66	-6.75	-8.03
Allyl chloride	-1.52	-2.85	-3.77
Amitrole	-2.66	-5.13	-6.36
Ammonium perfluorooctanoate	-4.31	-6.40	-7.55
Amyl methyl ether (tert-)	-0.09	-1.04	-1.96
Aniline	-0.17	-1.40	-2.44
Anisidine (o-)	-1.79	-2.30	-3.33
Anisidine (p-)	-1.80	-2.63	-3.67
ANTU	-2.21	-2.01	-2.99
Atrazine	-1.54	-3.57	-4.59
Biphenyl	-1.25	-2.39	-3.46
Bromacil	-0.80	-0.71	-1.61
Bromoform	-0.94	-2.52	-3.50
Butanol (sec-)	1.17	-0.08	-1.14
Butanol (tert-)	1.16	-0.45	-1.52
Butene	0.01	-1.19	-2.10
Butyl glycidyl ether (n-)	-0.34	-0.97	-1.96
Butyl lactate (n-)	-0.07	-0.55	-1.48
Butyl toluene (p-tert-)	-0.64	-2.68	-3.75
Camphor, synthetic	-0.47	-0.96	-1.88
Carbon disulfide	-1.52	-2.84	-3.75
Carbon monoxide	-0.34	-4.10	-5.40
Carbon tetrabromide	-1.52	-3.53	-4.49
Carbonyl fluoride	-1.93	-2.49	-3.39
Carbonyl sulfide	-2.00	-1.70	-2.61
Catechol	-0.07	-1.78	-2.70
Chlordane	-2.69	-5.50	-6.78

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Chlorinated camphene	-2.75	-6.56	-7.86
Chlorinated diphenyl oxide (o-)	-3.01	-5.98	-7.26
Chlorobenzene	0.30	-1.23	-2.21
Chlorobromomethane	1.26	-0.23	-1.17
Chlorodifluoromethane	0.16	-0.61	-1.52
Chloroform	-0.31	-1.58	-2.50
Chloropicrin	-2.62	-2.72	-3.62
Chlorostyrene (o-)	1.15	-0.80	-1.76
Citral	-0.12	-1.15	-2.18
Cumene	1.11	-0.86	-1.81
Cyclohexane	0.72	-1.02	-1.95
Cyclohexanol	0.88	0.15	-0.92
Cyclonite	-2.03	-2.29	-3.27
Cyclopentane	1.09	-0.38	-1.30
DDT	-2.37	-6.05	-7.35
Diacetyl	-2.82	-3.51	-4.53
Dibutyl phthalate	-1.36	-3.42	-4.54
Dichloroacetic acid	-1.07	-2.11	-3.09
Dichlorobenzene (o-)	0.85	-1.08	-2.04
Dichlorobenzene (p-)	0.43	-1.20	-2.20
Dichloroethyl ether	-0.11	-0.87	-1.90
Dichlorofluoromethane	-0.97	-2.18	-3.08
Dichloromethane	0.28	-0.97	-1.89
Dichlorotetrafluoroethane	0.21	-1.44	-2.36
Dieldrin	-3.38	-5.53	-6.70
Diethanolamine	-1.40	-2.58	-3.50
Diethyl ketone	1.52	1.69	0.79
Diethylene glycol monobutyl ether	0.21	-0.89	-1.92
Difluorodibromomethane	0.08	-1.94	-2.85
Diglycidyl ether (DGE)	-3.13	-5.26	-6.43
Diisopropylamine	0.21	-0.27	-1.29
Dimethyl disulfide	-1.10	-2.21	-3.18
Dimethylacetamide (N,N-)	-0.01	-2.07	-3.25
Dimethylaniline	0.22	-1.13	-2.15
Dimethylformamide	0.20	-1.53	-2.59
Dinitro-o-cresol	-2.40	-3.26	-4.29
Dinitrobenzene	-1.59	-1.33	-2.24
Dinitrobenzene (m-)	-1.61	-1.80	-2.84
Dinitrobenzene (o-)	-1.59	-1.33	-2.24
Dinitrobenzene (p-)	-1.59	-1.29	-2.19
Dinitrotoluene	-2.41	-3.39	-4.47
Diphenylamine	-0.40	-2.43	-3.45
Diquat	-2.91	-3.31	-4.21
Diquat	-3.34	-5.97	-7.22
Disulfiram	-1.26	-2.97	-3.96
Endosulfan	-3.06	-3.41	-4.51
Endrin	-3.38	-5.53	-6.70
Enflurane	-0.27	-1.35	-2.25
Epichlorohydrin	-1.16	-1.97	-3.00
Ethyl acrylate	-0.44	-1.07	-1.99
Ethyl amyl ketone	0.11	-0.74	-1.73

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Ethyl benzene	0.65	-1.08	-2.04
Ethyl bromide	-0.72	-2.33	-3.25
Ethyl butyl ketone	0.79	0.11	-0.86
Ethyl chloride	-0.68	-2.15	-3.07
Ethyl ether	0.97	0.03	-0.88
Ethyl mercaptan	-2.13	-2.87	-3.77
Ethyl morpholine (N-)	-0.19	-2.21	-3.35
Ethyl silicate	0.19	-0.10	-1.06
Ethyl tert-butyl ether	-0.12	-1.15	-2.06
Ethylene	-0.89	-1.94	-2.84
Ethylene dichloride	0.30	-1.71	-2.66
Ethylene glycol dinitrate (EGDN)	-2.07	-3.05	-3.99
Ethylenediamine	-0.43	-2.95	-4.19
Ethyleneimine	-1.77	-3.73	-4.72
Formamide	0.21	-1.28	-2.32
Glyoxal	-2.91	-5.97	-7.26
Halothane	-0.07	-1.87	-2.78
Heptachlor	-3.57	-6.05	-7.29
Heptachlor epoxide	-3.19	-5.27	-6.41
Heptane	0.89	-0.41	-1.33
Hexachlorobenzene	-4.24	-3.71	-4.67
Hexachlorobutadiene	-2.58	-4.72	-5.88
Hexachloroethane	-0.52	-2.50	-3.46
Hexachloronaphthalene	-3.03	-6.13	-7.41
Hexafluoroacetone	-3.91	-4.65	-5.55
Hexafluoropropylene	-5.15	-5.40	-6.30
Hexane (n-)	-0.41	-1.50	-2.40
Hydrogenated terphenyls	-1.48	-4.35	-5.63
Hydroquinone	-1.47	-1.95	-3.03
Indene	0.18	-1.70	-2.67
Iodoform	-0.88	-2.95	-4.07
Isobutene	0.11	-1.31	-2.22
Isopropyl acetate	0.90	-0.06	-0.98
Isopropylamine	0.06	-1.94	-2.99
Isopropylaniline (N-)	-0.26	-2.29	-3.33
Ketene	-1.92	-5.25	-6.54
Lindane	-2.26	-4.45	-5.62
Mesityl oxide	0.28	-0.59	-1.62
Methanol	1.49	-0.06	-1.10
Methoxychlor	-1.69	-4.92	-6.21
Methyl acetate	1.39	0.65	-0.27
Methyl acethylene	0.93	-0.22	-1.12
Methyl acrylate	-0.76	-1.58	-2.52
Methyl chloride	-0.30	-1.65	-2.56
Methyl chloroform	1.40	-0.62	-1.54
Methyl cyclohexane	1.32	-0.33	-1.26
Methyl cyclohexanone (o-)	0.88	0.12	-0.81
Methyl ethyl ketone (MEK)	1.39	0.39	-0.63
Methyl formate	0.55	-0.37	-1.31
Methyl iodide	-1.05	-2.80	-3.73
Methyl isoamyl ketone	0.36	-0.24	-1.20

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Methyl isobutyl carbinol	0.54	-0.17	-1.19
Methyl isobutyl ketone	0.25	-0.27	-1.24
Methyl isopropyl ketone	0.30	-0.43	-1.42
Methyl mercaptan	-2.18	-3.02	-3.92
Methyl methacrylate	0.49	-0.04	-0.97
Methyl n-butyl ketone	-0.24	-0.88	-1.85
Methyl silicate	-0.78	-1.25	-2.20
Methyl tert-butyl ether (MTBE)	0.28	-0.85	-1.77
Methylacrylonitrile	-0.83	-1.52	-2.47
Methylal	1.94	0.96	0.02
Methylaniline (N-)	-0.77	-1.94	-2.97
Metribuzin	-1.05	-2.49	-3.55
Morpholine	0.53	-1.04	-2.02
Naphthalene	0.47	-0.30	-1.39
Neopentane	-0.08	-0.77	-1.67
Nicotine	-2.22	-4.33	-5.49
Nitrapyrin	-0.54	-2.57	-3.59
Nitroaniline (p-)	-1.05	-0.99	-1.96
Nitrobenzene	-0.80	-0.92	-1.92
Nitrochlorobenzene (p-)	-1.85	-2.24	-3.34
Nitroethane	1.09	0.64	-0.39
Nitroglycerin (NG)	-2.07	-4.07	-5.01
Nitromethane	0.43	-0.19	-1.25
Nitrotoluene (m-)	-0.51	-1.19	-2.24
Nitrotoluene (o-)	-0.52	-1.29	-2.35
Nitrotoluene (p-)	-0.50	-1.00	-2.05
Nonane	1.15	-0.48	-1.41
Octachloronaphthalene	-3.43	-6.94	-8.24
Oxybis(p,p'-)	-2.94	-4.43	-5.41
Paraquat	-3.28	-5.68	-6.90
Pentachloronaphthalene	-2.47	-4.95	-6.19
Pentachloronitrobenzene	-2.26	-4.28	-5.26
Pentachlorophenol	-2.56	-4.74	-5.91
Pentane	0.60	-0.42	-1.32
Perfluorobutyl ethylene	-1.64	-3.67	-4.59
Phenol	-0.16	-1.55	-2.66
Phenyl ether, vapor	-0.89	-2.06	-3.13
Phenyl glycidyl ether	-1.80	-2.55	-3.59
Phenyl mercaptan	-1.51	-3.46	-4.42
Phenylenediamine (m-)	-2.43	-3.02	-4.03
Phenylenediamine (o-)	-2.41	-2.23	-3.13
Phthalonitrile (o-)	-1.35	-2.11	-3.27
Picloram	-0.99	-3.04	-4.20
Pindone	-3.35	-5.73	-6.94
Propargyl alcohol	-0.80	-2.02	-3.06
Propyl nitrate (n-)	0.18	-0.42	-1.32
Propylene	-0.04	-1.15	-2.06
Propylene dichloride	-1.55	-1.22	-2.12
Propylene glycol dinitrate	-2.12	-2.24	-3.14
Propyleneimine	-1.20	-3.20	-4.26
Pyridine	-0.49	-2.16	-3.18

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Quinone	-1.78	-1.50	-2.40
Rotenone	-1.99	-4.69	-5.96
Simazine	-2.07	-3.72	-4.72
Strychnine	-2.74	-3.22	-4.22
Styrene	0.73	-1.09	-2.06
Sulfometuron methyl	-1.24	-1.22	-2.12
Terephthalic acid	-0.87	-2.95	-4.11
Tetrachloroethylene	0.52	-1.35	-2.29
Tetrachloronaphthalene	-1.58	-3.73	-4.90
Tetrafluoroethylene	-3.37	-3.90	-4.80
Tetrahydrofuran	0.74	-0.75	-1.76
Tetramethyl succinonitrile	-1.09	-1.37	-2.40
Tetranitromethane	-3.13	-2.91	-3.81
Toluene	0.52	-1.00	-1.97
Toluidine (m-)	-0.19	-1.90	-2.89
Toluidine (o-)	-0.19	-1.89	-2.89
Toluidine (p-)	-0.17	-1.15	-2.20
Trichloronaphthalene	-0.86	-2.85	-3.90
Triethylamine	-0.91	-2.92	-3.88
Trifluorobromomethane	-0.58	-1.43	-2.34
Vinyl acetate	-0.36	-0.84	-1.74
Vinyl-2-pyrrolidone (N-)	-2.10	-3.21	-4.26
Vinylcyclohexene dioxide	-1.82	-3.31	-4.39
Vinylidene chloride	-0.83	-2.63	-3.55
Vinylidene fluoride	-0.73	-1.46	-2.36
Warfarin	-3.87	-3.52	-4.42
Xylene (m-)	1.38	-0.43	-1.39
Xylene (o-)	1.41	-0.59	-1.54
Xylene (p-)	1.37	-0.43	-1.39