APPENDIX A-4

TARGET ORGANS AND CRITICAL EFFECTS FOR COMPOUNDS WITH REFERENCE DOSE VALUES

TABLE A-4

TARGET ORGANS AND CRITICAL EFFECTS FOR COMPOUNDS WITH REFERENCE DOSE VALUES

Compound	CAS No.	Target Organ	Critical Effect
Acenaphthene	83-32-9	Liver	Hepatotoxicity
Acetone	67-64-1	Liver	Increased liver weights
		Kidney	Increased kidney weights and nephrotoxicity
Acetonitrile	75-05-8	Blood	Decreased red blood cell counts and hematocrit
		Liver	Hepatic lesions
Acetophenone	98-86-2	General	General toxicity
Acrolein	107-02-8	--	No adverse effects observed
Acrylonitrile	107-13-1	Reproductive	Decreased sperm counts, seminiferous tubule degeneration
Aldrin	309-00-2	Liver	Hepatotoxicity
Ammonia	7664-41-7	Sensory	Decreased taste threshold
Anthracene	120-12-7	--	No observed effects
Antimony	7440-36-0	Blood	Blood glucose and cholesterol, decreased longevity
Aroclor 1016	12674-11-2	Reproductive system	Decreased birth weights
Aroclor 1254	11097-69-1	Eye	Ocular exudate, inflamed and prominent meibomian glands
		General toxicity	Distorted growth of fingers and toenails
		Immune system	Decreased amtibody (IgM and IgG) response to sheep erythrocytes
Arsenic, inorganic	7440-38-2	Skin	Hyperpigmentation, keratosis, and possible vascular complications
Barium	7440-39-3	Blood pressure	Increased blood pressure
Benzaldehyde	100-52-7	Gastrointestinal	Forestomach lesions
		Kidney	Kidney toxicity
Benzidine	92-87-5	Liver	Liver cell alterations in females
		Nervous system	Brain cell vacuolization
Benzoic acid	65-85-0	--	No observed effects
Beryllium	7440-41-7	--	No adverse effects observed
Biphenyl, 1,1-	92-52-4	Kidney	Kidney damage
bis(2-Ethylhexyl)phthalate	117-81-7	Liver	Increased relative liver weight
bis(Chloromethyl)ether	542-88-1	--	No observed effects
Bromodichloromethane	75-27-4	Kidney	Renal cytomegaly
Bromoform	75-25-2	Liver	Hepatic lesions
Butyl benzyl phthalate	85-68-7	Liver	Significantly increased liver-to-body weight and liver-to-brain weight ratios

TABLE A-4 (Continued)

TARGET ORGANS AND CRITICAL EFFECTS FOR COMPOUNDS WITH REFERENCE DOSE VALUES

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Compound	CAS No.	Target Organ	Critical Effect
Cadmium	7440-43-9	Kidney	Significant proteinuria
Carbon disulfide	75-15-0	Reproductive	Fetal toxicity and malformations
Chlordane	57-74-9	Liver	Hepatocyte regeneration
Chlorine	7782-50-5	--	No observed effects
Chloroaniline, 4-	106-47-8	Spleen	Nonneoplastic lesions of the splenic capsule
Chlorobenzene	108-90-7	Liver	Histopathologic changes in liver
Chlorobenzilate	510-15-6	Gastrointestinal	Decreased stool quantity, food consumption, and body weight
		Nervous system	Hyperirritability
Chloroform	67-66-3	Liver	Fatty cyst formation in liver
Chloronaphthalene, 2-	91-58-7	Respiratory	Dyspnea, abnormal appearance, liver enlargement
Chlorophenol, 2-	95-57-8	Reproductive	Reproductive effects
Chlorotoluene, o-	95-49-8	Body weight	Decrease in body weight gain
Chlorpyrifos	2921-88-2	Blood	Decreased plasma cholinesterase activity
Chromium	7440-47-3	--	No observed effects
Chromium VI	18540-29-9	--	No observed effects
Cresol, o-(2-methylphenol)	95-48-7	Body weight	Decreased body weights
		Nervous system	Neurotoxicity
Cresol, p-	106-44-5	Whole body	Maternal death
		Nervous system	Hypoactivity
		Respiratory	Respiratory distress
Cumene	98-82-8	Kidney	Increased average kidney weight
Cyanide	57-12-5	--	No observed effects
Cyanogen	460-19-5	Body weight	Weight loss
		Nervous system	Myelin degeneration
		Thyroid	Thyroid effects
Cyanogen bromide	506-68-3	Body weight	Weight loss
		Nervous system	Myelin degeneration
		Thyroid	Thyroid effects
Cyanogen chloride	506-77-4	Body weight	Weight loss
		Neutroxicity	Myelin degeneration
		Thyroid	Thyroid effects

TABLE A-4 (Continued)

TARGET ORGANS AND CRITICAL EFFECTS FOR COMPOUNDS WITH REFERENCE DOSE VALUES

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Compound	CAS No.	Target Organ	Critical Effect
DDT, 4,4'-	50-29-3	Liver	Liver lesions
Demeton	8065-48-3	Nervous system	Cholinesterase inhibition
		Eye	Optic nerve degeneration
Diazinon	333-41-5	Blood	Decreased cholinesterase activity
Dibromochloromethane	124-48-1	Liver	Hepatic lesions
Dibromoethane, 1,2-	106-93-4	Reproductive system	Spermatogenic effects
Dibutyl phthalate	84-74-2	Death	Increased mortality
Dichlorobenzene, o-	95-50-1	--	No adverse effects observed
Dichlorodifluoromethane (CFC-12)	75-71-8	Body weight	Reduced body weight
Dichloroethane, 1,1-	75-34-3	--	No observed adverse effects (route-to-route extrapolation)
Dichloroethene, 1,1-	75-35-4	Liver	Hepatic lesions
Dichloroethene, trans-1,2-	156-60-5	Blood	Increased serum alkaline phosphatase in male mice
Dichloroethylene, cis-1,2-	156-59-2	Organ weight	Increased organ weight
		Respiratory	hypertrophy/hyperplasia of the nasal respiratory epithelium
Dichlorophenol, 2,4-	120-83-2	Immunotoxicity	Decreased delayed hypersensitivity response
Dichlorophenoxyacetic acid, 2,4- (2,4-D acid)	94-75-7	Blood	Hematologic toxicity
		Kidney	Hepatic toxicity
		Liver	Renal toxicity
Dichloropropene, 1,3-	542-75-6	Organ weights	Increased organ weights
Dichlorvos	62-73-7	Nervous system	Brain cholinesterase inhibition
		Blood	Plasma red blood cell cholinesterase inhibition
Dieldrin	60-57-1	Liver	Liver lesions
Diethyl phthalate	84-66-2	Body weight	Decreased growth rate and food consumption
		Organ weight	Altered organ weights
Dimethylphenol, 2,4-	105-67-9	General toxicity	Lethargy, prostration, ataxia,
		Blood	Hematological changes
Dimethylphthalate	131-11-3	Kidney	Kidney effects
Dinitrobenzene, 1,2-	528-29-0	Spleen	Increased spleen weight
Dinitrobenzene, 1,3-	99-65-0	Spleen	Increased spleen weight
Dinitrobenzene, 1,4-	100-25-4	Spleen	Increased spleen weight

TABLE A-4 (Continued)

TARGET ORGANS AND CRITICAL EFFECTS FOR COMPOUNDS WITH REFERENCE DOSE VALUES

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Compound	CAS No.	Target Organ	Critical Effect
Dinitro-o-cyclohexyl phenol, 4,6-	131-89-5	Eye	Cataract formation
Dinitrophenol, 2,4-	51-28-5	Eye	Cataract formation
Dinitrotoluene, 2,4-	121-14-2	Gastrointestinal	Heinze bodies and biliary tract hyperplasia
		Nervous system	Neurotoxicity
Dinitrotoluene, 2,6-	606-20-2	Death	Decreased survival
		Blood	Heinze bodies, methemoglobinemia
		Gastrointestinal	Hyperplasia of the bile duct
		Kidney	Histopathologic changes in the kidney
		Nervous system	Neurotoxic effects
Di-*n*-octyl phthalate	117-84-0	Kidney	Increased kidney weight
		Liver	Increased liver weight; increased SGOT and SGPT activity
Diphenylamine	122-39-4	Body weight	Decreased body weight gain
		Kidney	Increased kidney weight
		Liver	Increased liver weights
Disulfoton	298-04-4	Eye	Optic nerve degeneration
		Nervous system	Cholinesterase inhibition
Endosulfan I	115-29-7	Body weight	Decrease in body weight gain
		Nervous system	Neurotoxicity
		Kidney	Marked progressive glomerulonephrosis and blood vessel anurysms in males
Endothall	145-73-3	Gastrointestinal	Increased absolute and relative weights of stomach and small intestine
Endrin	72-20-8	Nervous system	Occasional convulsions
		Liver	Mild histological lesions
Epichlorohydrin	106-89-8	Kidney	Kidney lesions (route-to-route extrapolation)
Ethoxyethanol, 2-	110-80-5	Body weight	Decreased body weight
Ethylbenzene	100-41-4	Kidney	Kidney toxicity
		Liver	Liver toxicity
Ethylene glycol	107-21-1	Kidney	Kidney toxicity
Ethylene thiourea	96-45-7	Thyroid	Increased incidence of thyroid hyperplasia
Ethylmethacrylate	97-63-2	Kidney	Increased relative weight of the kidney

TABLE A-4 (Continued)

TARGET ORGANS AND CRITICAL EFFECTS FOR COMPOUNDS WITH REFERENCE DOSE VALUES

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Compound	CAS No.	Target Organ	Critical Effect
Fluoranthene	206-44-0	Blood	Hematological alterations and clinical effects
		Kidney	Nephropathy
		Liver	Increased liver weights
Fluorene	86-73-7	Blood	Decreased red blood cell count, packed cell volume and hemoglobin
Formaldehyde	50-00-0	Body weight	Reduced weight gain, histopathology in rats
Formic acid	64-18-6	Body weight	Decreased growth rate
Freon 113	76-13-1	Nervous system	Psychomotor impairment
Furan	110-00-9	Liver	Hepatic lesions
Furfural	98-01-1	Liver	Mild hepatocellular vacuolization
Glycidaldehyde	765-34-4	Adrenal	Enlarged adrenals
		Blood	Hydropic renal pelvis and hematopoietic effects
		Body weight	Retarded weight gain
Heptachlor	76-44-8	Liver	Liver weight increases in males only
Heptachlor epoxide	1024-57-3	Liver	Increased liver-to-body weight ratio
Hexachlorobenzene	118-74-1	Liver	Liver effects
Hexachlorobutadiene	87-68-3	Kidney	Renal tubules regeneration
Hexachlorocyclopentadiene	77-47-4	Gastrointestinal	Stomach lesions
Hexachloroethane	67-72-1	Kidney	Atrophy and degeneration of renal tubules
Hexachlorophene	70-30-4	Salivary gland	Swollen
		Brain and optic nerve	Status spongiosis
Hexane, n-	110-54-3	Nervous system	Neuropathy
		Respiratory	Epithilial lesions in the nasal cavity
Isophorone	78-59-1	Kidney	Kidney pathology
Malathione	121-75-5	Blood	Red blood cell cholinesterase depression
Maleic hydrazide	123-33-1	Kidney	Renal dysfunction
Malononitrile	109-77-3	Liver	Liver effects
		Spleen	Spleen effects
Manganese	7439-96-5	Nervous system	Central nervous system effects
Mercuric chloride	7787-94-7	Immune system	Autoimmune effects
Mercury (inorganic)	7439-97-6	Nervous system	Neurotoxicity
Merphos	150-50-5	Nervous system	Ataxia and delayed neurotoxicity

TABLE A-4 (Continued)

TARGET ORGANS AND CRITICAL EFFECTS FOR COMPOUNDS WITH REFERENCE DOSE VALUES

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Compound	CAS No.	Target Organ	Critical Effect
		Wholebody	Decreased body weight
Methacrylonitrile	126-98-7	Liver	Increased SGOT and SGPT levels
Methanol	67-56-1	Nervous system	Brain cholinesterase inhibition
		Blood	Plasma red blood cell cholinesterase inhibition
Methoxychlor	72-43-5	Reproductive	Excessive loss of litter
Methoxyethanol, 2-	109-86-4	Reproductive	Testicular effects (route-to-route extrapolation)
Methyl acetate	79-20-9	Liver	Increased alkaline phosphatase and increased SGPT
Methyl bromide	74-83-9	Gastrointestinal	Epithelial hyperplasia of the forestomach
Methyl ethyl ketone	78-93-3	Reproductive	Decreased fetal birth weight
Methyl isobutyl ketone	108-10-1	Kidney	Increased urinary protein
		Liver	Increased absolute and relative weights of the liver
		Nervous system	Lethargy
Methyl mercury	22967-92-6	Nervous system	Developmental neurological abnormalities in human infants
Methyl parathione	298-00-0	Blood	Red blood cell cholinesterase inhibition,reduced hemoglobin, hematocrit and red blood cells
Methyl styrene (mixed isomers)	25013-15-4	Respiratory	Nasal cavity lesions (route-to-route extrapolation)
Methylene bromide	74-95-3	Blood	Increased carboxyhemoglobin (route-to-route extrapolation)
Methylene chloride	75-09-2	Liver	Liver toxicity
Methylphenol, 3-(m-Cresol)	108-39-4	Body weight	Decreased body weights
		Nervous system	Neurotoxicity
Naled	300-76-5	Nervous system	Brain cholinesterase inhibition
Nickel, soluble salts	7440-02-0	Body weight	Decreased body weight
		Organ weight	Decreased organ weights
Nitroaniline, 2-	88-74-4	Blood	Hematological effects
Nitrobenzene	98-95-3	Adrenal	Adrenal lesions
		Blood	Hemolytic anemia
		Liver	Renal lesions
		Renal	Hepatic lesions
N-nitrosodi-*n*-propylamine	621-64-7	--	No observed adverse effects
Pentachlorobenzene	608-93-5	Kidney	Kidney toxicity

TABLE A-4 (Continued)

TARGET ORGANS AND CRITICAL EFFECTS FOR COMPOUNDS WITH REFERENCE DOSE VALUES

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Compound	CAS No.	Target Organ	Critical Effect
		Liver	Liver toxicity
Pentachloronitrobenzene	82-68-8	Liver	Hepatotoxicity
Pentachlorophenol	87-86-5	Kidney	Kidney pathology
		Liver	Liver pathology
Phenol	108-95-2	Reproductive	Reduced fetal body weight in rats
Phorate	298-02-2	Nervous system	Cholinesterase inhibition
Phthalic anhydride	85-44-9	Kidney	Histopathology
		Respiratory	Lung damage
Pronamide	23950-58-5	--	No observed effects
Propargyl alcohol	107-19-7	Kidney	Hepatotoxicity
		Liver	Renal toxicity
Propylene glycol monomethyl ether	107-98-2	Kidney	Histopathologic changes of the kidney
		Liver	Histopathologic changes of the liver
Pyrene	129-00-0	Kidney	Renal tubular pathology and decreased kidney weights
Pyridine	110-86-1	Liver	Increased liver weight
Ronnel	299-84-3	Liver	Liver effects
Selenium	7782-49-2	Respiratory	Clinical selenosis
Silver	7440-22-4	Skin	Argyria
Strychnine and salts	57-24-9	General	Toxicity and histopathology
Styrene	100-42-5	Blood	Red blood cell effects
		Liver	Liver effects
Tetrachlorobenzene, 1,2,4,5-	95-94-3	Kidney	Kidney lesions
Tetrachloroethane (carbon tetrachloride)	56-23-5	Liver	Liver lesions
Tetrachloroethane, 1,1,1,2-	630-20-6	Kidney	Mineralization of the kidneys in males
		Liver	Hepatic clear cell changes in females
Tetrachloroethene	127-18-4	Liver	Hepatotoxicity in mice, weight gain in rats
Tetrachlorophenol, 2,3,4,6-	58-90-2	Liver	Increased liver weight and centrilobular hypertrophy
Thallium	7440-28-0	Liver	Increased levels of SGOT and LDH
Toluene	108-88-3	Kidney	Changes in kidney weights
		Liver	Changes in liver weights

TABLE A-4 (Continued)

TARGET ORGANS AND CRITICAL EFFECTS FOR COMPOUNDS WITH REFERENCE DOSE VALUES

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Compound	CAS No.	Target Organ	Critical Effect
Toluene-2,6-diamine	823-40-5	--	No adverse effects observed
Trichlorobenzene, 1,2,4-	120-82-1	Adrenal	Increased adrenal weights; vacuolation of zona fasciculate in the cortex
Trichloroethane, 1,1,2-	79-00-5	Blood	Clinical serum chemistry
Trichlorofluoramethane (Freon 11)	75-69-4	Death	Decreased survival
		General	Histopathology
Trichlorophenol, 2,4,5-	95-95-4	Kidney	Kidney pathology
		Liver	Liver pathology
Trichloropropane, 1,2,3-	96-18-4	Blood	Alterations in clinical chemistry and reduction in red cell mass
Trinitrobenzene, sym-	99-35-4	Spleen	Increased spleen weight
Trinitrotoluene, 2,4,6-	118-96-7	Liver	Liver effects
Vinyl acetate	108-05-4	Body weight	Decreased body weight
		Kidney	Altered kidney weight
Xylenes	1330-20-7	Death	Increased mortality
		Body weight	Decreased body weight
		Nervous system	Hyperactivity
Xylene, m-	108-38-3	Death	Increase mortality
		Body weight	Decreased body weight
		Nervous system	Hyperactivity
Xylene, o-	95-47-6	Nervous system	Hyperactivity
Zinc	7440-66-6	Blood	47% decrease in erythrocyte superoxide dismutase concentration in females

Note:

Target organ and critical effect information presented in this table is intended only to provide the information needed to break down calculated hazard quotients for various chemicals, based on the target organs that they affect. The information is intended to be neither (1) an exhaustive list of the potential toxic effects of a compound, or (2) an indication that toxicological studies for a substance are inadequate because the target organ or critical effect for each particular substance is limited to one or two reported health effects. The noncancer reference dose (*RfD*) for ingestion exposure, or the reference concentration (*RfC*) for inhalation exposures, is generally based on the experimental dose that produces no adverse effects in the most sensitive laboratory animal tested (referred to as the no-observed-adverse effects-level [*NOAEL*]). If all of the doses used in experimental studies produce some effect, the lowest dose at which an adverse effect is observed (referred to as the lowest-observed-adverse-effect-level) is used to determine the *RfD* or *RfC*. Both uncertainty factors and modifying factors are included in the calculation of *RfDs* to ensure that these values are protective of human health (see Appendix A-3) (U.S. EPA 1988).

References:

U.S. Environmental Protection Agency (EPA) 1988. *Background Document—RfD Description and Use in Health Risk Assessments*.

U.S.EPA. 1995. "Health Effects Assessment Summary Tables."Fiscal Year-1995 Annual. Office of Solid Waste and Emergency Response. Washington, D.C. EPA/540/R-95/036. May.

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