APPENDIX G

TARGET ANALYTE DOSE-RESPONSE VARIABLES AND ASSOCIATED INFORMATION

Table G-1. Target Analyte Dose-Response Variables and Associated Information

Target analyte	Noncarcinogens: RfD[a] (degree of confidence; uncertainty factor)	Noncarcinogens: Critical toxic effect	Carcinogens: CSF[b] (discussion of confidence)	Carcinogens: Critical carcinogenic effect[c]	Carcinogens: EPA carcinogenicity classification[d]
Metals					
Arsenic (inorganic)	3×10^{-4} (medium; 3)	Hyperpigmentation, keratosis and possible vascular complications in humans	1.5	—	A
Cadmium	1×10^{-3} (high; 10)	Significant proteinurea in humans	NA	—	B1
Mercury (as methylmercury)	1×10^{-4} [e] (medium; 10)	Developmental neurological abnormalities in human infants	NA	—	C
Selenium[f]	5×10^{-3} (high; 3)	Selenosis in humans	NA	—	D
Tributyltin[g]	3×10^{-4} (high; 100)	Immunotoxicity in rats	NA	—	D
Organochlorine Pesticides					
Chlordane (sum of *cis*- and *trans*-chlordane, *cis*- and *trans*-nonachlor, and oxychlordane)[h]	5×10^{-4} (medium; 300)	Hepatic necrosis in mice	0.35 (Adequate number of animals observed. CSF is the geometric mean of CSFs for five data sets).	Hepatocellular carcinomas in 5 strains of mice (male and female)	B2
DDT (sum of 4,4'- and 2,4'- isomers of DDT, DDE, and DDD)[i]	5×10^{-4} (medium; 100)	Liver lesions in rats	0.34 (CSF is geometric mean of CSFs from 10 data sets.	DDT: Liver tumors in seven studies in various mouse strains and three studies in three rat strains	B2

See notes and references at end of table.

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Table G-1. (continued)

Target analyte	Noncarcinogens: RfD[a] (degree of confidence; uncertainty factor)	Noncarcinogens: Critical toxic effect	Carcinogens: CSF[b] (discussion of confidence)	Carcinogens: Critical carcinogenic effect[c]	Carcinogens: EPA carcinogenicity classification[d]
Dicofol	4×10^{-4} [j] (NA, 300)	Inhibition of ACTH stimulated release of cortisol in both sexes in 1-yr dog feeding study.	NA	—	C[k]
Dieldrin	5×10^{-5} (medium; 100)	Liver lesions (focal proliferation and focal hyperplasia) in one strain of female rats	16 (CSF is the geometric mean of CSFs from 13 data sets. Individual CSFs ranged within a factor of 8.)	Liver carcinomas in five strains of mice (male and female)	B2
Endosulfan (sum of endosulfan I and II)	6×10^{-3} (medium; 100)	Decreased body weight gain in male and female rat and progressive glomerulonephrosis and blood vessel aneurysms in one strain of male rats	NA	—	E[l]
Endrin	3×10^{-4} (medium; 100)	Mild histological lesions in livers, occasional convulsions in dogs (both sexes)	NA	—	D
Heptachlor epoxide	1.3×10^{-5} (low; 1000)	Increased liver-to-body weight ratios in male and female dogs	9.1 (Adequate number of animals observed in both studies, but survival in one study was low. This CSF is consistent with CSF = 5.8 for one strain of seven rats.)	Hepatocellular carcinomas in two strains of mice (male and female)	B2

See notes and references at end of table.

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Table G-1. (continued)

Target analyte	Noncarcinogens: RfD[a] (degree of confidence; uncertainty factor)	Noncarcinogens: Critical toxic effect	Carcinogens: CSF[b] (discussion of confidence)	Carcinogens: Critical carcinogenic effect[c]	Carcinogens: EPA carcinogenicity classification[d]
Hexachlorobenzene	8×10^{-4} (medium; 100)	Liver effects (hepatic centrilobular basophilic chromogenesis) in one strain of rats (both sexes)	1.6 (Significant increases in malignant tumors observed among an adequate number of animals observed for their lifetime.)	Hepatocellular carcinomas in one strain of rats (females only)	B2
Lindane (γ-HCH)	3×10^{-4} (medium; 1,000)	Liver and kidney toxicity (liver hypertrophy, kidney tubular degeneration, hyaline droplets, tubular distension, interstitial nephritis, and basophilic tubules) in both sexes of one strain of rats	1.3[m]	—	B2/C[l]
Mirex	2×10^{-4} (high; 300)	Liver cytomegaly, fatty metamorphosis, angiectasis and thyroid cystic follicles in one strain of rats.	NA	—	B2[m]
Toxaphene	2.5×10^{-4} [n] (NA, 1,000)	Slight liver degeneration—granularity and vacuolization of hepatocytes.	1.1 (Adequate number of animals observed. A dose-response effect was seen in a study with three non-zero dose levels.)	Hepatocellular carcinomas and neoplastic nodules in one strain of mice (males only)	B2

See notes and references at end of table.

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Table G-1. (continued)

Target analyte	Noncarcinogens: RfD[a] (degree of confidence; uncertainty factor)	Noncarcinogens: Critical toxic effect	Carcinogens: CSF[b] (discussion of confidence)	Carcinogens: Critical carcinogenic effect[c]	Carcinogens: EPA carcinogenicity classification[d]
Organophosphate Pesticides					
Chlorpyrifos	3×10^{-4} [o] (NA, 10)	Decreased plasma ChE activity observed in various animal feeding studies.	NA	—	E[o]
Diazinon	7×10^{-4} [p] (NA, 30)	Inhibition of plasma ChE observed in 90-d rat feeding study.	NA	—	Not likely E[l]
Disulfoton	4×10^{-5} (medium, 100)	ChE inhibition and degeneration of the optic nerve observed in 2-yr rat feeding study.	NA	—	E[l]
Ethion	5×10^{-4} (medium, 100)	Plasma ChE inhibition (in 21-d human feeding study) and inhibition of brain ChE observed in 90-d dog feeding study.	NA	—	E[l]
Terbufos	2×10^{-5} [q] (NA, 300)	Inhibition of plasma ChE observed in 28-d dog feeding study.	NA	—	E[l]
Chlorophenoxy Herbicides					
Oxyfluorfen	3×10^{-3} (high, 100)	Increased absolute liver weight and nonneoplastic lesions observed in 20-mo mouse feeding study.	7.32×10^{-2} [l]	Evidence of carcinogenicity (liver tumors) in mice.	C[l]

See notes and references at end of table.

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Table G-1. (continued)

Target analyte	Noncarcinogens: RfD[a] (degree of confidence; uncertainty factor)	Noncarcinogens: Critical toxic effect	Carcinogens: CSF[b] (discussion of confidence)	Carcinogens: Critical carcinogenic effect[c]	Carcinogens: EPA carcinogenicity classification[d]
PAHs[r]					
Benzo[*a*]pyrene	NA	—	7.3 (Data less than optimal, but acceptable. Four data sets used from two different studies using two different species (rats and mice; both sexes) to derive geometric mean of four calculated slope factors.)	Squamous cell carcinoma of the forestomach in one strain of mice (both sexes). Forestomach, larynx, and esophagus papillomas and carcinomas in one strain of rats (both sexes)	B2
PCBs					
Total PCBs (sum of Aroclors)	2×10^{-5} [s] (medium; 300)	Ocular exudate, inflamed, prominent Meibomian glands, distorted growth of fingernails, and toenails, decreased antibody response to sheep erythrocytes in monkey clinical and immunologic studies	2.0[t] (Adequate number of animals observed for their normal lifespan. Only one non-zero test dose used.)	Trabecular carcinomas/adenocarcinomas, neoplastic nodules in one strain of rats (females only)	B2
Dioxins/furans	NA	—	1.56×10^{5} [u]	NA	B2[u]

NA = Not available in IRIS (1992).
PAHs = Polycyclic aromatic hydrocarbons.
PCBs = Polychlorinated biphenyls.
DDT = p,p'-Dichlorodiphenyl trichloroethane.
DDD = p,p'-Dichlorodiphenyl dichloroethylene.
DDE = p,p'-Dichlorodiphenyl trichloroethane.

See notes and references at end of table.

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Table G-1. (continued)

[a] RfD = Oral reference dose (mg/kg-d); from IRIS (1999) unless otherwise noted (see Section 5.1.1).

[b] CSF = Oral cancer slope factor $(mg/kg\text{-}d)^{-1}$; from IRIS (1999) unless otherwise noted (see Section 5.1.2).

[c] The critical effect is the effect observed in oral dose response studies used to determine the CSF.

[d] Except where noted, all EPA carcinogenicity classifications are taken from IRIS (1999):

- A = Human carcinogen based on sufficient evidence from epidemiologic studies.
- B1 = Probable human carcinogen based on limited evidence of carcinogenicity to humans.
- B2 = Probable human carcinogen based on sufficient evidence in animals and inadequate or no data in humans.
- C = Possible human carcinogen based on limited evidence of carcinogenicity in animals in the absence of human data.
- D = Not classifiable based on lack of data or inadequate evidence of carcinogenicity from human or animal data.
- E = No evidence of carcinogenicity for humans (no evidence of carcinogenicity in at least two adequate animal tests in different species or in both epidemiologic and animal studies).

[e] The RfD for methylmercury should be considered an interim value. The National Academy of Sciences (NAS) conducted an independent assessment of the RfD and concluded, "On the basis of its evaluation, the committee consensus is that the value of EPA's current RfD for a scientifically justifiable level for the protection of human health." (NAS 2000).

[f] The evidence of carcinogenicity for various selenium compounds in animals and mutagenicity studies is conflicting and difficult to interpret. However, evidence for selenium sulfides is sufficient for a B2 classification (IRIS, 1999).

[g] The oral RfD and cancer classification are for tributyltin oxide (IRIS, 1999).

[h] The RfD and CSF values listed are derived from studies using technical-grade chlordane (IRIS, 1999) for the *cis*- and *trans*-chlordane isomers or the major chlordane metabolite, oxychlordane, or for the chlordane impurities *cis*- and *trans*-nonachlor. It is recommended that the total chlordane concentration be determined by summing the individual concentrations of *cis*- and *trans*-chlordane, *cis*- and *trans*-nonachlor, and oxychlordane.

[i] The RfD value listed is for DDT. The CSF value is for total DDT (sum of DDT, DDE, and DDD) or DDE; the CSF value for DDD is 0.24. The U.S. EPA Carcinogenicity Assessment Group recommended the use of CSF = 0.34 for any combination of DDT, DDE, DDD, and dicofol (Holder, 1986). It is recommended that the total concentration of the 2,4'- and 4,4'-isomers of DDT and its metabolites, DDE and DDD, be determined.

[j] The RfD value is from a memorandum dated December 12, 1997. Dicofol: Report of the Hazard Identification Assessment Review Committee. HED Document No. 012439 (U.S. EPA, 1997b).

[k] EPA carcinogenicity classification based on Reregistration Eligibility Decision (RED) Dicofol (U.S. EPA, 1998b).

[l] EPA carcinogenicity classification based on U.S. EPA, (1999).

[m] EPA CSF based on HEAST (1997).

[n] Reference dose information is taken from the Office of Pesticide Programs Reference Dose Tracking Report (U.S. EPA, 1997a).

[o] Oral RfD based on the Revised Human Health Risk Assessment for Chlorpyrifos (U.S. EPA, 2000).

[p] The RfD value is from a memorandum dated April 1, 1998, Diazinon: Report of the Hazard Identification Assessment Review Committee. HED Doc. No. 012558 (U.S. EPA, 1998a).

[q] The RfD value listed is from a memorandum dated September 25, 1997; Terbufos-FQPA Requirement- Report of the Hazard Identification Review. (U.S. EPA, 1997c).

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[r] This CSF is for benzo[*a*]pyrene (IRIS, 1999). There are no other RfDs or CSFs listed for other PAHs in IRIS (1999). It is recommended that, tissue samples be analyzed for benzo[*a*]pyrene and 14 other PAHs (Nisbet and LaGoy, 1992; U.S. EPA, 1993) and that the order-of-magnitude relative potencies given for these PAHs be used to calculate a potency equivalency concentration (PEC) for each sample for comparison with the recommended SV for benzo[*a*]pyrene (see Section 5.3.2.4).

[s] This RfD for PCBs is based on the chronic toxicity of Aroclor 1254 (IRIS, 1999).

[t] This CSF is based on a carcinogenicity assessment of Aroclor 1260, 1254, 1242, and 1016. The CSF represented is the upper bound slope factor for food chain exposure. The central estimate is 1.0 (IRIS, 1999).

[u] The CSF value listed is for 2,3,7,8-tetrachlorodibenzo-p-dioxin 2,3,7,8-TCDD (HEAST, 1997). It is recommended that, in both screening and intensive studies, the 17 tetra- through octa-chlorinated dibenzo-p-dioxins (PCDDs) and dibenzofurans (PCDFs) and the 12 dioxin-like PCBs be determined and a toxicity-weighted total concentration be calculated for each sample for comparison with the recommended SV, using the method for estimating Toxicity Equivalency Concentration (TEQ) (Van den Berg et al., 1998).

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