Table 5-21. Illustrative RfDs based on hypothesized key events in TCDD's MOAs for liver and lung tumors (REVISED 10-1-2010)

Key event	Endpoint and exposure duration	$NO(A)EL_{HED}$ (ng/kg-day)	$LO(A)EL_{HED}$ (ng/kg-day)	$BMDL_{HED}$[a] (ng/kg-day)	RfD[b] (mg/kg-day)	Study
Liver tumors						
Changes in gene expression	CYP1A1 mRNA, 1 day	**3.1E−05**	7.0E−04	1.4E−03[c] (Appendix H)	1E−12[d,e]	Vanden Heuvel et al. (1994, 594318)
Changes in gene expression	Benzo(a)pyrene hydroxylase (BPH) activity (CYP1A1), 1 day	**3.3E−04**	1.9E−03	7.7E−03[c,d] (Appendix H)	1E−11[d,e]	Kitchin and Woods (1979, 198750)
	EROD (CYP1A1), 53 weeks	none	**1.0E−01**	5.8E−04[c] (Appendix H)	3E−10[f]	NTP (2006, 197605)
Oxidative stress	DNA single-strand breaks, 90 days	none	**7.0E−02**	6.3E−03[c] (Appendix H)	2E−10[f]	Hassoun et al. (2000, 197431)
	TBARS, 90 days	**7.0E−02**	2.7E−01	5.3E−02[c] (Appendix H)	2E−09[e]	Hassoun et al. (2000, 197431)
	Cytochrome C reductase, 90 days	7.0E−02	2.7E−01	**1.2E−01** (Appendix H)	4E−09[e]	Hassoun et al. (2000, 197431)
Hepatotoxicity	Toxic hepatopathy, 2 years	none	**1.4E−01**	1.8E−01 (Appendix E)	1E−09[g]	NTP (2006, 197605)
	Hepatocyte hypertrophy, 31 weeks	none	**9.3E−02**	1.7E−02[c] (Appendix E)	6E−10[e]	NTP (2006, 197605)
Hepatocellular proliferation	Labeling index, 31 weeks	none	**9.3E−02**	1.5E−01[c] (Appendix H)	3E−10[e]	NTP (2006, 197605)
Lung tumors						
Metabolic enzyme induction	EROD (CYP1A1), 53 weeks	none	1.0E−01	**2.9E−04** (Appendix H)	1E−11[e]	NTP (2006, 197605)
Retinoid homeostatsis	Hepatic retinol, 90 days	none	5.3E-01	**1.7E−01** (Appendix E)	6E−09[e]	Van Birgelen et al. (1995, 198052)

[a]BMR for continuous endpoints—1 standard deviation; for quantal endpoints—10%.
[b]Bolded NOAEL, LOAEL, or BMDL is selected POD; poorly-fitting BMDLs above the LOAEL not used.
[c]Poor BMD model fit or lack of response near BMR.
[d]Could be higher depending on the effect of background exposure (see Section 5.3.2.1).
[e]UF = 30; UF_A = 3; UF_H = 10.
[f]UF = 300; UFA = 3; UFH = 10; UFL = 10.
[g]UF = 100; UFA = 3; UFH = 10; UFL =