APPENDIX – G: Chronic Toxicity Values

Table G1. Cancer and Noncancer Toxicity Values for COPCs: Inhalation Unit Risk (IUR) and Chronic Reference Level (RfC).

COMPOUND	CANCER		NONCANCER	
	IUR (μg per $m^3)^{-1}$	Cancer classification	Chronic RfC ($\mu g/m^3$)	Target organ (*Critical and other effects*)
Acetaldehyde	0.0000022 I	Probable human carcinogen (B2) *Nasal and laryngeal tumors in animals*	9.0 I	Respiratory *(Degeneration of Olfactory epithelium)*
Acetone	NC	NC	30880.0 A	Neurological *(delayed visual reaction, general weakness, headache)*
1,3-Butadiene	0.00003 I	Known human carcinogen (A) *Lymphohematopoietic cancer and leukemia in humans*	2.0 I	Reproductive *(Ovarian atrophy)*
Benzene*	0.0000078 I	Known human carcinogen (A) Leukemia in humans	30.0* I	Immunological *(Decreased lymphocyte count)*
Crotonaldehyde	0.000543 [a] H	Possible human carcinogen (C) *Hepatic neoplastic nodules and hepatocellular carcinoma in animals (oral study)*	NA	NA
Cyclohexane	NC	NC	6000.0 I	Reproductive/developmental *(Reduced pup weight)*
Ethylbenzene	0.0000025 C	Probable human carcinogen (B2) Renal tumors in animals	1000.0 I	Developmental *(Kit mortality)*
Formaldehyde**	0.000013 I	Probable human carcinogen (B1) *Nasopharyngeal and lung cancer in humans (limited) and nasal cancer in animals*	9.8** A	Respiratory *(Histopathological changes in nasal tissue in humans)*
n-Hexane	NC		700.0 I	Neurological *(Peripheral neuropathy)*

Table G1. Continued

COMPOUND	CANCER		NONCANCER	
	IUR (μg per m^3)$^{-1}$	**Cancer classification**	**Chronic RfC ($\mu g/m^3$)**	**Target organ (*Critical and other effects*)**
Isopropylbenzene (cumene)	NC	NC	400.0 I	Renal/Adrenal *(Increased kidney and adrenal weight)*
Methylcyclo-hexane	NC	NC	3010.0 H	Renal *(Mineralization, papillary hyperplasia in animals)*
Nonane	NC	NC	200.0 P	Salivation, lacrimation, and reduced body weight
n-Pentane	NC	NC	1000.0 [d] P	Neurologic
Propionaldehyde	NC	NC	8.0 I	Respiratory *(Atrophy of olfactory epithelium)*
Propylene	NC	NC	3000.0 C	Respiratory *(Squamous metaplasia, epithelial hyperplasia, and inflammation of the nasal cavity in animals)*
Propylbenzene	NC	NC	1000.0 P	Derived using ethylbenzene as a surrogate
Styrene	NC	NC	1000.0 I	Neurological *(Increase in reaction time, decreased memory, impaired visual perception)*
Toluene	NC	NC	5000.0 I	Neurological and respiratory *(Neurological effects; other effects: degeneration of nasal epithelium)*
1,2,3-Trimethyl benzene	NC	NC	5.0 [c] P	Neurologic , respiratory and hematological (*Decreased pain sensitivity*)
1,2,4-Trimethyl benzene	NC	NC	7.0 [c] P	Neurologic, Respiratory, and hematologic *(Decreased blood clotting time)*
1,3,5-Trimethyl benzene	NC	NC	20.0 [b] Draft I	Neurologic, Respiratory, and hematologic (*Decreased pain sensitivity)*
o-Xylene/m-Xylene/p-Xylene	NC	NC	100.0 I	Neurologic *(Impaired motor coordination)*

Table G1. Continued

COMPOUND	CANCER		NONCANCER	
	IUR (μg per m^3) $^{-1}$	**Cancer classification**	**Chronic RfC ($\mu g/m^3$)**	**Target organ (*Critical and other effects*)**
Aliphatic hydrocarbons C5-C8	0.00000019 P	Suggestive evidence Pituitary adenoma or carcinoma (screening value[e])	600.0 P	Nasal epithelial cell hyperplasia
Aliphatic hydrocarbons C9-C18	0.0000045 P	Suggestive evidence Benign or malignant adrenal pheochromocytoma (screening value[e])	100.0 P	Nasal goblet cell hypertrophy and adrenal hyperplasia
Aromatic hydrocarbons C9-C16	NC		100.0 P	Maternal body weight depression

Note:

- Under the 2005 EPA guidelines for carcinogenic assessment, Class A carcinogens = carcinogenic to humans; Class B1 and B2 = Likely to be carcinogenic to humans; Class C = suggestive evidence of carcinogenic potential
- Sources of toxicity values: A= ATSDR Minimal Risk Level (MRL); C = Cal EPA; H= EPA-HEAST; I- EPA IRIS; P= PPRTV
- *ATSDR chronic MRL for benzene is 9.6 $\mu g/m^3$ and the impact of this value will be discussed qualitatively.
- ** Formaldehyde toxicity assessment is under evaluation by USEPA IRIS. According to USEPA's 2010 draft assessment and the NRC/NAS (2014), formaldehyde is a known human carcinogen via inhalation. In addition, it is a mutagenic carcinogen with the draft IUR of 1.1 x10-4 per $\mu g/m^3$. A range of draft RfC is also developed by the USEPA IRIS (3 to13.5 $\mu g/m^3$).

NC = Non-Carcinogen; NA= Not Available

[a] Based on route-to-route extrapolation of EPA's oral cancer slope factor
[b] Based on draft 2012 EPA IRIS external peer review document. This value is subject to change based on external peer review comments
[c] These values may change to 20.0 $\mu g/m^3$ based on draft 2012 EPA IRIS external peer review document
[d] Threshold for toxic effects of *n*-pentane is not established. PPRTV is based on a NOAEL based on the neurotoxicity and developmental toxicity studies in animals which showed negative findings
[e] Screening PPRTVs are developed by EPA where a high degree of uncertainty exists. These values are intended for use in limited circumstances when no other values are available (US EPA, 2009)