APPENDIX H

H.1. Lifetable Analysis:

A spreadsheet illustrating the extra risk calculation for the derivation of the LEC_{01} for RCC incidence is presented in Table H-1.

Table H-1. Extra risk calculation[a] for environmental exposure to 1.82 ppm TCE (the LEC_{01} for RCC incidence)[b] using a linear exposure-response model based on the categorical cumulative exposure results of Charbotel et al. (2006), as described in Section 5.2.2.1.2.

A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P
Interval number (i)	Age interval	All cause mortality ($\times 10^5$/yr)	RCC incidence ($\times 10^5$/yr)	All cause hazard rate (h*)	Prob of surviving interval (q)	Prob of surviving up to interval (S)	RCC cancer hazard rate (h)	Cond prob of RCC incidence in interval (R0)	Exp duration mid interval (xtime)	Cum exp mid interval (xdose)	Exposed RCC hazard rate (hx)	Exposed all cause hazard rate (h*x)	Exposed prob of surviving interval (qx)	Exposed prob of surviving up to interval (Sx)	Exposed cond prob of RCC in interval (Rx)
1	<1	685.2	0	0.0069	0.9932	1.0000	0.000000	0.000000	0.5	2.77	0.000000	0.0069	0.9932	1.0000	0.000000
2	1-4	29.9	0	0.0012	0.9988	0.9932	0.000000	0.000000	3	16.61	0.000000	0.0012	0.9988	0.9932	0.000000
3	5-9	14.7	0	0.0007	0.9993	0.9920	0.000000	0.000000	7.5	41.52	0.000000	0.0007	0.9993	0.9920	0.000000
4	10-14	18.7	0.1	0.0009	0.9991	0.9913	0.000005	0.000005	12.5	69.20	0.000006	0.0009	0.9991	0.9913	0.000006
5	15-19	66.1	0.1	0.0033	0.9967	0.9903	0.000005	0.000005	17.5	96.88	0.000006	0.0033	0.9967	0.9903	0.000006
6	20-24	94	0.2	0.0047	0.9953	0.9871	0.000010	0.000010	22.5	124.56	0.000013	0.0047	0.9953	0.9871	0.000013
7	25-29	96	0.7	0.0048	0.9952	0.9824	0.000035	0.000034	27.5	152.24	0.000049	0.0048	0.9952	0.9824	0.000048
8	30-34	107.9	1.6	0.0054	0.9946	0.9777	0.000080	0.000078	32.5	179.91	0.000117	0.0054	0.9946	0.9777	0.000114
9	35-39	151.7	3.2	0.0076	0.9924	0.9725	0.000160	0.000155	37.5	207.59	0.000245	0.0077	0.9924	0.9724	0.000237
10	40-44	231.7	6.3	0.0116	0.9885	0.9651	0.000315	0.000302	42.5	235.27	0.000504	0.0118	0.9883	0.9650	0.000484
11	45-49	352.3	11	0.0176	0.9825	0.9540	0.000550	0.000520	47.5	262.95	0.000919	0.0180	0.9822	0.9537	0.000869
12	50-54	511.7	17.3	0.0256	0.9747	0.9373	0.000865	0.000801	52.5	290.63	0.001507	0.0262	0.9741	0.9367	0.001393
13	55-59	734.8	26.2	0.0367	0.9639	0.9137	0.001310	0.001175	57.5	318.31	0.002375	0.0378	0.9629	0.9124	0.002127
14	60-64	1140.1	36.2	0.0570	0.9446	0.8807	0.001810	0.001549	62.5	345.99	0.003409	0.0586	0.9431	0.8786	0.002909
15	65-69	1727.4	44.6	0.0864	0.9173	0.8319	0.002230	0.001777	67.5	373.67	0.004358	0.0885	0.9153	0.8286	0.003456
16	70-74	2676.4	49	0.1338	0.8747	0.7631	0.002450	0.001750	72.5	401.35	0.004961	0.1363	0.8726	0.7584	0.003518
17	75-59	4193.2	51.6	0.2097	0.8109	0.6675	0.002580	0.001554	77.5	429.03	0.005407	0.2125	0.8086	0.6617	0.003223
18	80-84	6717.2	44.4	0.3359	0.7147	0.5412	0.002220	0.001021	82.5	456.71	0.004809	0.3384	0.7129	0.5351	0.002183
							Ro =	0.010736						**Rx =**	0.020586
extra risk = (Rx−Ro)/(1−Ro) = 0.00996															

Column A: interval index number (i).
Column B: 5-year age interval (except <1 and 1−4) up to age 85.
Column C: all-cause mortality rate for interval i ($\times 10^5$/year) (2004 data from NCHS).
Column D: RCC incidence rate for interval i ($\times 10^5$/year) (2001-2005 SEER data).
Column E: all-cause hazard rate for interval i (h^*_i) (= all-cause mortality rate × number of years in age interval).[c]
Column F: probability of surviving interval i without being diagnosed with RCC (q_i) (= $\exp(-h^*_i)$).
Column G: probability of surviving up to interval i without having been diagnosed with RCC (S_i) ($S_1 = 1$; $S_i = S_{i-1} \times q_{i-1}$, for i>1).
Column H: RCC incidence hazard rate for interval i (h_i) (= RCC incidence rate × number of years in interval).
Column I: conditional probability of being diagnosed with RCC in interval i (= $(h_i/h^*_i) \times S_i \times (1-q_i)$), i.e., conditional upon surviving up to interval i without having been diagnosed with RCC [Ro, the background lifetime probability of being diagnosed with RCC = the sum of the conditional probabilities across the intervals].
Column J: exposure duration (in years) at mid-interval (xtime).
Column K: cumulative exposure mid-interval (xdose) (= exposure level (i.e., 1.82 ppm) × 365/240 × 20/10 × xtime) [365/240 × 20/10 converts continuous environmental exposures to corresponding occupational exposures].
Column L: RCC incidence hazard rate in exposed people for interval i (hx_i) (= $h_i \times (1 + \beta \times \text{xdose})$, where $\beta = 0.001205 + (1.645 \times 0.0008195) = 0.002554$) [0.001205 per ppm × year is the regression coefficient obtained from the weighted linear regression of the categorical results (see Section 5.2.2.1.2). To estimate the LEC_{01}, i.e., the 95% lower bound on the continuous exposure giving an extra risk of 1%, the 95% upper bound on the regression coefficient is used, i.e., MLE + 1.645 × SE].
Column M: all-cause hazard rate in exposed people for interval i (h^*x_i) (= $h^*_i + (hx_i - h_i)$).
Column N: probability of surviving interval i without being diagnosed with RCC for exposed people (qx_i) (= $\exp(-h^*x_i)$).
Column O: probability of surviving up to interval i without having been diagnosed with RCC for exposed people (Sx_i) ($Sx_1 = 1$; $Sx_i = Sx_{i-1} \times qx_{i-1}$, for i>1).
Column P: conditional probability of being diagnosed with RCC in interval i for exposed people (= $(hx_i/h^*x_i) \times Sx_i \times (1-qx_i)$) [Rx, the lifetime probability of being diagnosed with RCC for exposed people = the sum of the conditional probabilities across the intervals].

[a] Using the methodology of BEIR IV (1988).
[b] The estimated 95% lower bound on the continuous exposure level of TCE that gives a 1% extra lifetime risk of RCC.
[c] For the cancer incidence calculation, the all-cause hazard rate for interval i should technically be the rate of either dying of any cause or being diagnosed with the specific cancer during the interval, i.e., (the all-cause mortality rate for the interval + the cancer-specific incidence rate for the interval—the cancer-specific mortality rate for the interval [so that a cancer case isn't counted twice, i.e., upon diagnosis and upon death]) × number of years in interval. This adjustment was ignored here because the RCC incidence rates are small compared with the all-cause mortality rates.
MLE = maximum likelihood estimate, SE = standard error.

H.2. Equations Used for Weighted Linear Regression of Results from Charbotel et al. (2006):

[source: Rothman (1986), p. 343-344]

linear model: RR = 1 + bX

where RR = risk ratio, X = exposure, and b = slope

b can be estimated from the following equation:

$$\hat{b} = \frac{\sum_{j=2}^{n} w_j x_j R\hat{R}_j - \sum_{j=2}^{n} w_j x_j}{\sum_{j=2}^{n} w_j x_j^2}$$

where j specifies the exposure category level and the reference category (j = 1) is ignored.

the standard error of the slope can be estimated as follows:

$$SE(\hat{b}) \approx \sqrt{\frac{1}{\sum_{j=2}^{n} w_j x_j^2}}$$

the weights, w_j, are estimated from the confidence intervals (as the inverse of the variance):

$$Var(R\hat{R}_j) \approx R\hat{R}_j^{\,2} Var[\ln(R\hat{R}_j)] \approx R\hat{R}_j^{\,2} \times \left[\frac{\ln(\overline{RR}_j) - \ln(\underline{RR}_j)}{2 \times 1.96} \right]^2$$

where $\overline{RR}_j$ is the 95% upper bound on the RR_j estimate (for the jth exposure category) and $\underline{RR}_j$ is the 95% lower bound on the RR_j estimate.