

Date: 14 March 2007

To: Interested Persons
From: DEQ Toxicology Workgroup
Subject: Incorporation of Early-Life Exposure in Human Health Risk Assessments

Background

In March 2005, EPA issued new *Guidelines for Carcinogenic Risk Assessment* (EPA/630/P-03/001B), updating the 1986 guidelines and 1999 interim final guidelines. Also included was *Supplemental Guidance for Assessing Susceptibility from Early-Life Exposure to Carcinogens* (EPA/630/R-03/003F). In a 29 March 2005 memorandum on Application of New Cancer Guidelines, then Acting Administrator Stephen Johnson stated that:

1. For all¹ newly initiated carcinogenicity risk assessments, the Cancer Guidelines and Supplemental Guidance will be used from this point forward;
2. For risk assessments currently being performed, the guidance will be used on a case-by-case basis; and
3. For completed risk assessments, reassessments may be performed on a case-by-case basis when a new decision is required that needs to be supported by an updated risk assessment. Until that time, the current completed risk assessment will continue to be considered scientifically sound based on the guidance used when the assessment was completed.

DEQ typically follows EPA risk assessment guidance. In the *Supplemental Guidance*, EPA concludes that some chemicals (carcinogens acting by a mutagenic mode of action) have a greater cancer impact if exposure occurs during childhood. This changes the way DEQ will perform risk assessments involving residential exposure. Cancer risk will now be evaluated using different adjusted potency factors for three life stages (0 – 2 years, 2 – 16 years, and adult). We currently use only one potency factor for two life stages (child 0 – 6 years, and adult).

EPA created workgroups to provide additional information on how to implement the Supplemental Guidance, and provide consistency. One outcome of the workgroups is an EPA memorandum clarifying which chemicals should be evaluated for early-life exposure². The list of chemicals is provided in Table 1. EPA determined that vinyl chloride should continue to be evaluated using the specific procedure for evaluating early-life exposure developed about four years ago. We have applied the procedure in our risk assessments since then, and included it in our 2003 revisions to the risk-based decision making (RBDM) guidance. The only other early-life chemicals of interest to the cleanup program are the carcinogenic polycyclic aromatic hydrocarbons (cPAHs).

¹ Emphasis in original.

² EPA Memorandum dated 14 June 2006: Implementation of the Cancer Guidelines and Accompanying Supplemental Guidance – Science Policy Council Cancer Guidelines Implementation Workgroup Communication II: Performing Risk Assessments that Include Carcinogens Described in the Supplemental Guidance as having a Mutagenic Mode of Action.

EPA is still in the process of finalizing guidance on the exposure parameters to be used in an evaluation of early-life exposure. In the interim, DEQ consulted with EPA Region 10. EPA Region 10 is now using screening values developed by EPA Region 6. EPA Region 6 includes an evaluation of early-life exposure in calculating their screening values. Until EPA develops a national set of exposure values, we will use the assumptions of early-life exposure used by EPA Region 6.

DEQ is now requiring the consideration of early-life exposure on all human health risk assessments for sites where the relevant exposure scenarios include residential site use or other uses where childhood exposure is likely. In conjunction, we have developed risk-based concentrations (RBCs) for vinyl chloride and cPAHs based on early-life exposure. In the future, if EPA includes additional chemicals for early-life consideration, the appropriate RBC screening values can be calculated using the RBC spreadsheet. To activate the early-life option, go to the Toxicological Data sheet, and change the Early Life designation from “n” to “y”. Then click the Recalculate button to automatically calculate RBCs based on early-life exposure.

Revisions to Risk Assessment Calculations

Risk assessments for carcinogens acting by a mutagenic mode of action will now include a new term called an age dependent adjustment factor (ADAF) to account for increased carcinogenic potency during early life stages. For ages up to 2 years, the ADAF is 10, indicating a ten-fold increase in carcinogenic potency during this period. For ages from 2 years to 16 years, the ADAF is 3. For ages 16 years and older, the ADAF is 1. Using ADAFs, the differences in potency are incorporated by a factor separate from the slope factor, so only one cancer slope factor is needed. Risk assessments for carcinogens that do not act by a mutagenic mode of action should be conducted as before, using the slope factor without adjustments for age.

In developing exposure parameters for children, EPA decided that it would be more accurate to divide the 2- to 16-year-old stage into two stages (2 to 6 years, and 6 to 16 years). Both stages have the same ADAF value, but body weights, skin surface area, and intakes differ.

The incorporation of ADAFs is best included in the calculation of age-adjusted intake factors. These factors are used both in forward risk assessments and calculations of RBCs. Equations for age-adjusted intake factors are presented on page A-2 in Appendix A of DEQ's *Guidance for Conduct of Deterministic Human Health Risk Assessments* (1998), and on page B-26 of DEQ's *Risk-Based Decision Making Guidance for the Remediation of Petroleum-Contaminated Site* (2003). For carcinogens acting by a mutagenic mode of action, these equations should be modified as follows:

Soil ingestion

$$IRS_{adj} = \frac{ED_2 \cdot IRS_2 \cdot ADAF_2}{BW_2} + \frac{ED_6 \cdot IRS_6 \cdot ADAF_6}{BW_6} + \frac{ED_{16} \cdot IRS_{16} \cdot ADAF_{16}}{BW_{16}} + \frac{ED_{adult} \cdot IRS_{adult} \cdot ADAF_{adult}}{BW_{adult}}$$

Water ingestion

$$IRW_{adj} = \frac{ED_2 \cdot IRW_2 \cdot ADAF_2}{BW_2} + \frac{ED_6 \cdot IRW_6 \cdot ADAF_6}{BW_6} + \frac{ED_{16} \cdot IRW_{16} \cdot ADAF_{16}}{BW_{16}} + \frac{ED_{adult} \cdot IRW_{adult} \cdot ADAF_{adult}}{BW_{adult}}$$

Soil dermal contact

$$SFS_{adj} = \frac{ED_2 \cdot AF_2 \cdot SA_2 \cdot ADAF_2}{BW_2} + \frac{ED_6 \cdot AF_6 \cdot SA_6 \cdot ADAF_6}{BW_6} + \frac{ED_{16} \cdot AF_{16} \cdot SA_{16} \cdot ADAF_{16}}{BW_{16}} + \frac{ED_{adult} \cdot AF_{adult} \cdot SA_{adult} \cdot ADAF_{adult}}{BW_{adult}}$$

Water dermal contact

$$SAS_{adj} = \frac{ED_2 \cdot SA_2 \cdot ADAF_2}{BW_2} + \frac{ED_6 \cdot SA_6 \cdot ADAF_6}{BW_6} + \frac{ED_{16} \cdot SA_{16} \cdot ADAF_{16}}{BW_{16}} + \frac{ED_{adult} \cdot SA_{adult} \cdot ADAF_{adult}}{BW_{adult}}$$

Inhalation

$$INF_{adj} = \frac{ED_2 \cdot IRA_2 \cdot ADAF_2}{BW_2} + \frac{ED_6 \cdot IRA_6 \cdot ADAF_6}{BW_6} + \frac{ED_{16} \cdot IRA_{16} \cdot ADAF_{16}}{BW_{16}} + \frac{ED_{adult} \cdot IRA_{adult} \cdot ADAF_{adult}}{BW_{adult}}$$

where:

- IRS_{adj} = Age-adjusted incidental soil ingestion factor ([mg·yr]/[kg·d])
- IRW_{adj} = Age-adjusted water ingestion factor ([L·yr]/[kg·d])
- SFS_{adj} = Age-adjusted soil dermal contact factor ([mg·yr]/[kg·event])
- SAS_{adj} = Age-adjusted water dermal contact factor ([cm²·yr]/kg)
- INF_{adj} = Age-adjusted inhalation factor ([m³·yr]/[kg·d])
- ADAF₂ = Age-dependent Adjustment Factor, child 0 to <2 years old (unitless)
- ADAF₆ = Age-dependent Adjustment Factor, child 2 to <6 years old (unitless)
- ADAF₁₆ = Age-dependent Adjustment Factor, child 6 to <16 years old (unitless)
- ADAF_{adult} = Age-dependent Adjustment Factor, adult (unitless)
- ED₂ = Exposure duration, child 0 to <2 years old (yr)
- ED₆ = Exposure duration, child 2 to <6 years old (yr)
- ED₁₆ = Exposure duration, child 6 to <16 years old (yr)
- ED_{adult} = Exposure duration, adult (yr)
- BW₂ = Body weight, child 0 to <2 years old (kg)
- BW₆ = Body weight, child 2 to <6 years old (kg)
- BW₁₆ = Body weight, child 6 to <16 years old (kg)
- BW_{adult} = Body weight, adult (kg)

IRS ₂	=	Soil ingestion rate, child 0 to <2 years old (mg/d)
IRS ₆	=	Soil ingestion rate, child 2 to <6 years old (mg/d)
IRS ₁₆	=	Soil ingestion rate, child 6 to <16 years old (mg/d)
IRS _{adult}	=	Soil ingestion rate, adult (mg/d)
IRW ₂	=	Water ingestion rate, child 0 to <2 years old (L/d)
IRW ₆	=	Water ingestion rate, child 2 to <6 years old (L/d)
IRW ₁₆	=	Water ingestion rate, child 6 to <16 years old (L/d)
IRW _{adult}	=	Water ingestion rate, adult (L/d)
AF ₂	=	Adherence factor, child 0 to <2 years old (mg/cm ² ·event)
AF ₆	=	Adherence factor, child 2 to <6 years old (mg/cm ² ·event)
AF ₁₆	=	Adherence factor, child 6 to <16 years old (mg/cm ² ·event)
AF _{adult}	=	Adherence factor, adult (mg/cm ² ·event)
SA ₂	=	Exposed skin surface area, 0 to <2 years old child (cm ²)
SA ₆	=	Exposed skin surface area, 2 to <6 years old child (cm ²)
SA ₁₆	=	Exposed skin surface area, child 6 to <16 years old (cm ²)
SA _{adult}	=	Exposed skin surface area, adult (cm ²)
IRA ₂	=	Inhalation rate, child 0 to <2 years old (m ³ /d)
IRA ₆	=	Inhalation rate, child 2 to <6 years old (m ³ /d)
IRA ₁₆	=	Inhalation rate, child 6 to <16 years old (m ³ /d)
IRA _{adult}	=	Inhalation rate, adult (m ³ /d)

The default parameter values are shown in Table 2.

Implementation Schedule

DEQ will follow the same general implementation approach used by EPA. Early-life exposure will be incorporated into risk assessments, and screening levels based on early-life exposure will be applied using the following guidelines:

1. For all newly initiated carcinogenicity risk assessments, the approach for incorporating early-life exposure presented in this memorandum will be used from this point forward;
2. For risk assessments currently being performed, the early-life guidelines will be used on a case-by-case basis; and
3. For completed risk assessments submitted before 2 April 2007, reassessments may be performed on a case-by-case basis when a new decision is required that needs to be supported by an updated risk assessment. Until that time, the current completed and approved risk assessment will continue to be considered scientifically sound based on the guidance used when the assessment was completed.

DEQ will routinely update RBC screening values in January of each year. Under special circumstances, RBCs for a chemical may be updated at any time based on revised toxicity information.

Table 1
Chemicals Determined by EPA to be Carcinogens Having a Mutagenic Mode of Action

Chemical ^a	Chemical Abstract Service Registration Number
Chemicals typically found at Cleanup Program sites	
Benz[a]anthracene ^b	56-55-3
Benzo[b]fluoranthene ^b	205-99-2
Benzo[k]fluoranthene ^b	207-08-9
Benzo[a]pyrene	50-32-8
Chrysene ^b	218-01-9
Dibenz[a,h]anthracene	53-70-3
Dimethylbenz[a]anthracene	57-97-6
Indeno[1,2,3-cd]pyrene ^b	193-39-5
Vinyl chloride ^c	75-01-4
Chemicals not typically found at Cleanup Program sites	
Benzidine	92-87-5
N-Nitrosodiethylamine (diethylnitrosamine)	55-18-5
N-Methyl-N-nitrosomethanamine (dimethylnitrosamine)	62-75-9
N-Nitrosoethylurea (ethylnitrosourea)	759-73-9
3-Methylcholanthrene	56-49-5
N-Nitroso-N-methylurea (methylnitrosourea)	684-93-5
Safrole	94-59-7
Urethane (ethyl carbamate)	51-79-6

Notes:

- a) Source: EPA Memorandum dated 14 June 2006: Implementation of the Cancer Guidelines and Accompanying Supplemental Guidance – Science Policy Council Cancer Guidelines Implementation Workgroup Communication II: Performing Risk Assessments that Include Carcinogens Described in the Supplemental Guidance as having a Mutagenic Mode of Action.
- b) Although not explicitly included in EPA’s list, EPA states that carcinogenic PAHs with a relative potency factor relating the toxicity to the slope factor for benzo[a]pyrene should also be evaluated for early-life exposure.
- c) Early-life exposure to vinyl chloride should be evaluated using the chemical-specific analysis presented in EPA’s Integrated Risk Information System (www.epa.gov/iris), and not by using the general ADAF approach. The appropriate IRIS method is used to calculate RBC values for vinyl chloride.

Table 2
Default Parameter Values for Early-Life Exposure

Parameter	<2 Years Old	2 to <6 Years Old	6 to <16 Years Old	Adult
ADAF (unitless) ^a	10	3	3	1
ED (yr)	2	4	10	14 ^b
BW (kg) ^c	15	15	70	70
IRS (mg/d) ^c	200	200	100	100
IRW (L/d) ^c	1	1	2	2
AF (mg/cm ² ·event) ^d	0.2	0.2	0.07	0.07
SA (cm ²) ^c	2,800	2,800	5,700	5,700
IRA (m ³ /d) ^c	10	10	20	20

Notes:

- a) ADAF values taken from *Supplemental Guidance for Assessing Susceptibility from Early-Life Exposure to Carcinogens* (EPA/630/R-03/003F, March 2005).
- b) The standard residential default exposure duration is 30 years. For adult ED, DEQ uses 30 years minus the time exposed as a child, for a total of 14 years as an adult.
- c) Exposure values taken from *Exposure Factors Handbook* (EFH) (EPA/600/P-95/002F, 1997) and *Risk Assessment Guidance for Superfund, Volume I, Human Health Evaluation Manual (Part A)* (EPA/540/1-89/002, Interim Final, December 1989).
- d) Adherence factors taken from p. 3-17 and Exhibit C-3 of *Risk Assessment Guidance for Superfund: Volume I – Human Health Evaluation Manual (Part E, Supplemental Guidance for Dermal Risk Assessment)*, EPA/540/R/99/005, Interim Review Draft, 2001.