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Memorandum

Air Quality Program

February 14, 2019

To: 460 Rulemaking Stakeholders

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Subject: Use of early-life adjustment factors in deriving acceptable source impact levels for a subset of toxic air pollutants

In 2005, the USEPA developed Supplemental Guidance for Assessing Susceptibility from Early-Life Exposure to Carcinogens (EPA 2005). As its name suggests, this guidance supplemented existing risk assessment guidance, and addressed the potential for increased susceptibility to cancer caused by exposures to environmental chemicals during an early lifestage. EPA determined that chemicals that cause cancer through a mutagenic mode of action can have greater toxicity during early-life stages. Because many unit risk values were derived from toxicity studies involving mature lifestage animals, EPA determined that early-life adjustment factors were necessary to account for increased susceptibility among infants and children exposed to mutagenic chemicals.

The following age dependent adjustment factors are used for exposures occurring at different lifestages:

- A factor of 10 for infants up to 2 years old
- A factor of 3 for children aged 2 to 16
- No adjustment is used for people aged 16 and above

Deriving ASILs for chemicals that cause cancer through a mutagenic mode of action.

ASILs are derived to be a concentration that results in an increased lifetime cancer risk of 1 in one million assuming continuos lifetime (i.e., assumed to be 70 yrs) exposure. To account for

exposures occurring in early life, early-life adjustment factors are factored into the ASIL derivation:

$$\text{ASIL} = \frac{\text{target cancer risk}}{\text{URF x ELAF}}$$

Where:

ASIL = Acceptable source impact level ($\mu g/m^3$)
Target cancer risk = 1 in one million lifetime cancer risk
URF = Unit risk factor $(\mu g/m^3)^{-1}$
ELAF = Early-life adjustment factor

The early-life adjustment factor for continuous lifetime exposure is derived using the following age dependent adjustment factors:

Ages	**Duration (years)**	**Age dependent adjustment factor (ADAF)**
Infant to < 2	2	10
2 to < 16	14	3
16 to 70	54	1

Early-life adjustment factor for lifetime exposure

$$= \frac{[ADAF_{(\text{infant to } <2)} \text{ x } 2 \text{ yrs}] + [ADAF_{(2 \text{ to } <16)} \text{ x } 14 \text{ yrs}] + [ADAF_{(16 \text{ to } 70)} \text{ x } 54 \text{ yrs}]}{70 \text{ yrs}}$$

$$= 10 \times \frac{2}{70} + 3 \times \frac{14}{70} + 1 \times \frac{54}{70}$$

= **1.66**

Chemicals considered to cause cancer through the mutagenic mode of action

Ecology relied on the following three EPA documents to determine which pollutants act through the mutagenic mode of action.

EPA Supplemental Guidance for Assessing Susceptibility from Early-Life Exposure to Carcinogens

EPA's "Supplemental Guidance for Assessing Susceptibility from Early-Life Exposure to Carcinogens" specified that the following chemicals "are associated with mutagenicity":

- Benzidine
- Benzo(a)pyrene
- Dibenz(a,h)anthracene

- 7-12-dimethylbenz(a)anthracene
- 3-methylcholanthrene
- N-nitrosodiethylamine
- N-nitrosodimetylamine
- N-nitroso-N-ethylurea
- N-nitroso-N-methylurea
- Safrole
- Urethane
- Vinyl chloride

EPA's Integrated Risk Information System

Subsequent chemical assessments as part of EPA's Integrated Risk Information System identified the following additional chemicals that act through a mutagenic mode of action:

- Acrylamide
- Ethylene oxide
- Methylene chloride
- Trichloroethylene
- 1,2,3-trichloropropane
- Chloroprene

EPA's Regional Screening Level – User's Guide

Finally, EPA's "Regional Screening Level – User's Guide" lists the following additional chemicals as mutagens:

- Benz(a)anthracene
- Benzo(b)fluoranthene
- Bnezo(k)fluoranthene
- Chromium VI
- Chrysene
- Coke oven emissions
- 1,2-Dibromo-3-chloropropane
- Indeno(1,2,3-cd)pyrene
- 2,4'-methylene-bis(2-chloraniline)

Early-life adjustment factor for trichloroethylene (TCE)

EPA developed several unit risk factors for trichloroethylene (TCE) based on liver cancer, non-Hodgkins lymphoma, and kidney cancer (EPA 2011). A single unit risk factor for estimating total cancer risk from exposure to TCE can determined by summing each of the URFs. Because EPA determined that TCE acts though a mutagenic mode of action for kidney tumors, but not other cancers, age-dependent adjustment factors apply only to kidney cancer portion of the total cancer risk estimate.

The following shows the early-life adjustment factor for TCE is estimated to be:

Cancer type	Inhalation unit risk factor	Early-life adjusted unit risk factor
Renal cell carcinoma (kidney)	1×10^{-6} per µg/m^3	1.7×10^{-6} per µg/m^3
Non-Hodgkins lymphoma	2×10^{-6} per µg/m^3	NA
Liver cancer	1×10^{-6} per µg/m^3	NA
All cancers	4×10^{-6} per µg/m^3	4.7×10^{-6} per µg/m^3

Early-life adjustment factor for lifetime TCE exposure =

Early-life adjusted unit risk / Unadjusted unit risk

= 4.7×10^{-6} per µg/m^3 / 4×10^{-6} per µg/m^3

= **1.2**

Early-life adjustment factor for vinyl chloride

In the IRIS documentation for vinyl chloride, EPA provided two separate unit risk factors: one for inhalation exposure beginning as an adult, and one for lifetime exposures beginning at birth (EPA 2000). These values differ by a factor of two as shown below:

Inhalation Unit Risk

4.4×10^{-6} per µg/m^3 (continuous lifetime exposure during adulthood)
8.8×10^{-6} per µg/m^3 (continuous lifetime exposure from birth)

No early-life adjustment factor was used to derive the vinyl chloride ASIL because we used the unit risk factor for continuous lifetime exposure from birth.

References

EPA 2000. United States Environmental Protection Agency. Integrated Risk Information System (IRIS) Chemical Assessment Summary for Vinyl Chloride. Date last revised 8/7/2000. Available at URL: https://cfpub.epa.gov/ncea/iris/iris_documents/documents/subst/1001_summary.pdf

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EPA 2011. United States Environmental Protection Agency. Integrated Risk Information System (IRIS) Chemical Assessment Summary for Trichlorethylene. Date last revised 9/28/2011. Available at URL: https://cfpub.epa.gov/ncea/iris/iris_documents/documents/subst/0199_summary.pdf

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