To: Salyer, Kathleen[Salyer.Kathleen@epa.gov]
Cc: Stralka, Daniel[Stralka.Daniel@epa.gov]; Lee, Alana[lee.alana@epa.gov]
From: Hiatt, Gerald
Sent: Wed 9/4/2013 11:58:50 PM
Subject: Use of the TCE RfC in calculating Hazard Quotients for less-than-continuous exposures

Kathleen, The 2001 IRIS toxicity re-assessment of TCE established a reference concentration (RfC) to be protective for non-cancer health effects. Three non-cancer health effects were identified as critical: kidney toxicity, immunotoxicity and congenital heart defects (CHDs) in offspring of women exposed to TCE during pregnancy. The first 2 non-cancer end-points (kidney and immune) were identified by toxicity studies involving both chronic (lifetime or a significant fraction thereof) and sub-chronic (days to weeks) exposures. In contrast, CHD risk arises only from a sub-chronic exposure (the approximately 3 weeks during development of the heart in a fetus). RfCs are traditionally thought of as screening levels primarily for chronic exposures because they are usually based on a toxic end-point arising as a result of a chronic exposure.

Risk-based screening levels. For a continuous exposure (e.g., as is assumed for residential), the non-cancer risk-based screening level then becomes the RfC, based on a Hazard Quotient of 1 (HQ=1). However, when exposure is less-than-continuous (e.g. a workplace exposure) an appropriate HQ=1 risk-based screening level is calculated by adjusting the RfC for the relevant exposure frequency and duration. The default exposure assumptions for a workplace are 8 hours/day for 250 days/year (2 weeks of vacation/holiday are assumed).

With respect to the risk of CHDs caused by maternal exposure to TCE, the relevant critical period of exposure corresponds to the 3 weeks (21 days) of cardiac organogenesis during the first trimester of pregnancy. For continuous (e.g., residential) exposures, no time-weighted adjustment to the RfC is needed and the appropriate risk-based screening level is the RfC itself = 2 ug/m3. For workplace exposures, the less-than-continuous time-weighting adjustment must take the 21 day critical period into account. Assuming an 8 hour workday, 5 day workweek and no holidays taken during the critical period, the calculation of a risk-based screening level protective for women of reproductive age in the workplace is:

(Total hours) / (Hours exposed) x RfC

(21 days x 24 hours/day) / (15 days x 8 hours/day) x 2 ug/m3 = 8.4 ug/m3; rounded to 1 significant digit = 8 ug/m3

Note that the workplace calculation is slightly different if one is considering an end-point arising from a chronic exposure (e.g., a year-long exposure; 365 days):

(Total hours) / (Hours exposed) x RfC

(365 days x 24 hours/day) / (250 days x 8 hours/day) x 2 ug/m3 = 8.8 ug/m3; rounded to 1 significant digit = 9 ug/m3

I hope this helps illustrate how the 21 day critical period for cardiac organogenesis affects the calculation of a risk-based screening level for less-than-continuous exposures.

Gerry

P.S. The internal review version of the IRIS addendum addressing CHD risks from maternal TCE exposure notes the following:

The TCE chronic RfC is a reasonable choice for estimating HQs for subchronic exposures (greater than 24 hours up to approximately 10% of the life span) to women of childbearing age. Specifically, a reasonable choice for the exposure duration of concern is the 3-week period of major cardiac morphogenesis, and this duration period can be used for calculating the time-weighted average EC [exposure concentration] for comparison with the RfC.

Gerald F.S. Hiatt, Ph.D.

Senior Regional Toxicologist

U.S. EPA, Regon 9

(415) 972-3064

hiatt.gerald@epa.gov

Please be advised I am currently unable to access email from outside the office (e.g., when on travel), therefore please be patient with any communication delays