

On the RfD

1. The Mocarelli et al. (2008) and Baccarelli et al. (2008) studies (based on the Seveso accident) were selected as cocritical studies for the derivation of the RfD. Given that these studies involve subchronic exposures and the RfD is for chronic exposures, is the rationale for this selection scientifically justified and clearly described? Please identify and provide the rationale for any other human studies that should be selected, including the rationale for why the study would be considered a superior candidate for the derivation of the chronic RfD. Add on to the next question

On the cancer potency

5.d. Due to nonlinearities in the Emond PBPK model (specifically pertaining to the relationship between exposure and internal dose), EPA calculated a series of risk-specific oral slope factors. The calculation of multiple slope factors has not been done before. Please comment on EPA's rationale for and presentation of these slope factors. Does the calculation of multiple slope factors present a *de facto* assumption of low-dose nonlinearity, and if so, would it be preferable for EPA to use the same approach, i.e., estimation of a reference dose (RfD) from a point of departure (POD), that it has used for other chemicals in the IRIS database?

From: Johnson, Mark S Dr CIV USA MEDCOM PHC
Sent: Tuesday, May 18, 2010 12:52 PM
To: Meyer, Anita K HNC@NWO; Kurtz, Katharine M. (CIV); Putzrath, Resha (CIV)
Cc: Boyd, Robert, Mr, OSD-ATL
Subject: RE: NCEA Interagency Communication #68 (draft revised charge for dioxin SAB review) - no change in due date (UNCLASSIFIED)

Classification: UNCLASSIFIED
Caveats: NONE

I would like to know further their logic for the log-linear extrapolation from the various PODs. To do so assumes that even one molecule has a risk associated with it (that one molecule can cause cancer). Their logic in the documentation is that cancer is AhR-mediated (bc non Ahr-effects occur at much higher exposures). If that is their supposition, then it is receptor mediated and must function as a promoter (like a hormone); therefore must have a threshold. The NAS asked the EPA to provide a different curve beyond the POD, and the EPA argued that because they do not have enough info, they will use the conservative approach. However, that is not what the science suggests. I would suggest a curve similar to the phorbol esters, which function in a similar, yet conservative manner, but never got that far in the phonecon.

Sorry for this long message, but I would ask the SAB if they feel that the

EPAs logic for the log-linear extrapolation from the POD is justified.

Thanks,
Mark