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Re: Draft Reanalysis of Key Issues Related to Dioxin Toxicity and Response to NAS
Comments, 75 Fed. Reg. 28610 (May 21, 2010), Docket ID No. EPA-HQ-ORD-2010-0395

Dear Drs. Clark and Armitage:

On July 9th, the General Electric Company (GE) submitted preliminary comments on EPA's *Draft Reanalysis of Key Issues Related to Dioxin Toxicity and Response to NAS Comments* (Draft Reanalysis). In its comments, GE explained that EPA intends to apply the Cancer Slope Factor and non-cancer Reference Dose derived in the Draft Reanalysis for 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD) to other "dioxin-like compounds" (DLCs), including the so-called dioxin-like polychlorinated biphenyls (PCBs), through the use of the "toxic equivalency factors" (TEFs) derived by the World Health Organization (WHO) (WHO2005 TEFs).¹ We noted that the National Academy of Sciences (NAS) committee that reviewed the 2003 draft Dioxin Reassessment concluded that the use of the WHO TEFs might give rise to substantial errors, in part because the WHO TEFs assume that the potencies of the DLCs do not vary between species. We then provided substantial evidence that dioxin and PCBs are far less potent in humans than in the rodents from which the WHO TEFs were primarily derived.

GE's written comments were followed by a brief presentation to the panel at its public meeting in July by Dr. Jay Silkworth. He presented research that indicates that humans are an order of magnitude less responsive to dioxin, and even less responsive to PCB 126, than responsive rodents and monkeys. Dr. Silkworth's research also indicates that there is a threshold for the induction of effects by both dioxin and PCB 126. Additional research that reinforces this evidence has just been accepted for publication. *Analysis of the CYP1A1 mRNA Dose Response in Human Keratinocytes*

¹ See EPA's September, 2009 draft Guidance on Recommended Toxicity Equivalency Factors (TEFs) for Human Health Risk Assessments of Dioxin and Dioxin-like Compounds, 74 Fed. Reg. 45437 (Sept. 2, 2009); see also EPA's January, 2010 Draft Recommended Interim Preliminary Remediation Goals for Dioxin in Soil at Superfund and RCRA sites, 75 Fed. Reg. 984 (January 7, 2010).

Indicates that Relative Potencies of Dioxins, Furans, and PCBs are Species and Congener Specific, C. H. Sutter; S. Bodreddigari; T. R. Sutter; E. A. Carlson; J. B. Silkworth Toxicological Sciences 2010; doi:10.1093/toxsci/kfq262 . GE will provide copies of this study after it is formally published to EPA and to Dr. Armitage for distribution to the panel.

It is unclear whether the panel will address the issues surrounding the use of the WHO TEFs. At the public meeting in July, a number of panel members questioned EPA's focus on TCDD *per se*, when dioxin is often found in mixtures with other DLCs, and studies cited in the Draft Reanalysis include the DLCs. Dr. Peter Preuss, who at the time was the Director of the National Center for Environmental Assessment, acknowledged that TEFs are an important issue, but stated that TEFs are not part of the Draft Analysis. He also expressed the hope that the TEFs would not be part of the panel's deliberations. The panel, however, can go beyond EPA's charge if the panel believes that it is appropriate to do so. See Risk Policy Report, *Delay In SAB Report On EPA Arsenic Risk Study May Boost Industry Critic* (June 18, 2010)(reporting that SAB cochair Dr. Deborah Swackhammer stated that the panel reviewing EPA's draft risk assessment for inorganic arsenic has "the purview to make statements beyond the charge.")

All of the effort to determine accurate risk values for dioxin will be of little value if the panel, through silence, appears to sanction EPA's use of inappropriate, uncorrected WHO2005 TEFs to evaluate the toxicity of mixtures of dioxins and DLCs, particularly PCBs. Thus, at minimum, the SAB review panel should recommend that EPA refrain from applying the WHO2005 TEFs to the DLCs, including PCBs, unless and until EPA implements the NAS recommendations relating to TEFs and derives TEFs that incorporate newer, more accurate estimates of the human-specific relative potency of the DLCs, particularly PCBs.

If the panel chooses not to address the TEF issues, the panel nevertheless should take Dr. Silkworth's research into account in determining whether EPA had adequate scientific justification for rejecting the NAS panel's unanimous conclusion that "the scientific evidence, based largely on mode of action, is adequate to favor the use of a nonlinear model that would include a threshold response over the default linear assumption." National Academy of Sciences (NAS). 2006. *Health Risks from Dioxin and Related Compounds: Evaluation of the EPA Reassessment*, pp. 122, 190. Committee on EPA's Exposure and Human Health Reassessment of TCDD and Related Compounds, National Research Council of the National Academies. Washington, DC.

Thank you for your consideration of these comments.

Sincerely,

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