Texas Commission on Environmental Quality
Comments Regarding the U.S. Environmental Protection Agency
Draft EPA's Reanalysis of Key Issues Related to
Dioxin Toxicity and Response to NAS Comments
Notice of Public Comment Period
75 FR 28610, May 21, 2010
Docket ID No. EPA-HQ-ORD-2010-0395

On May 21, 2010, the U.S. Environmental Protection Agency (EPA) published a Federal Register notice (Federal Register/Vol. 75, No. 98/Friday, May 21, 2010/Notices) of a 90-day public comment period (ending August 19, 2010) for the, "Draft EPA's Reanalysis of Key Issues Related to Dioxin Toxicity and Response to NAS Comments," hereafter referred to as the draft reanalysis (EPA/600/R-10/038A). EPA will only guarantee that comments submitted by July 7, 2010, will be provided to the Scientific Advisory Board (SAB) in time for their panel meeting for independent external peer review of the draft reanalysis. The draft reanalysis: (1) details EPA's technical response to the key comments and recommendations included in the 2006 National Academy of Sciences (NAS) report, "Health Risks from Dioxin and Related Compounds: Evaluation of the EPA Reassessment," with a focus on dose-response issues; (2) classifies 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD or dioxin) as carcinogenic to humans; (3) provides an oral slope factor for TCDD; and (4) provides an oral reference dose (RfD) for TCDD, although EPA has not historically calculated an RfD. The Texas Commission on Environmental Quality (TCEQ) has developed comments on the draft reanalysis to the extent practicable in the time allotted by EPA and provides the following limited comments for EPA consideration.

General Comment:

The assessment of the carcinogenic and non-carcinogenic potential of TCDD has great implications both in a regulatory context and in the public's perception of risk. Given their important role in the protection of public health, EPA regulatory risk assessors have a duty to perform the most scientifically defensible assessments possible while giving careful and due consideration to comments and recommendations from other regulatory agencies, the public, external experts such as NAS, stakeholders, etc. Although regulatory risk assessors have a penchant for erring on the side of health-protectiveness and conservative defaults, if erring on the side of conservatism significantly overestimates risk or hazard and is not fully justified, then harm to public health may result from diverting public, industry, and government attention and resources away from chemicals that may represent more of a public health risk at environmental levels. Therefore, TCEQ encourages EPA to give full, thoughtful, and careful consideration and evaluation to comments and recommendations from TCEQ, other regulatory agencies, the public, and external experts such as NAS despite the artificial imposition of a December 31, 2010, deadline for release of the final TCDD reassessment.

90-Day Comment Period:

The 90-day comment period is insufficient for regulatory agencies and others to provide thorough and meaningful comments based on an in-depth review and analysis of the draft reanalysis. There is great complexity associated with multiple issues relevant to the

assessment of TCDD risk and hazard due to oral exposure. The draft reanalysis alone is 1,850 pages, with the SAB comments relevant to EPA's draft reanalysis being another 268 pages, and hundreds of pages of other documents (e.g., EPA draft for NAS review, EPA response to NAS review document) and studies relevant to the assessment of TCDD risk and hazard due to oral exposure. Given the complexity and volume of relevant materials, it is impracticable for EPA to expect detailed specific comments from external experts given the short period allowed for a critical review of the draft reanalysis and procedures employed by EPA. The 90-day comment period only allows a very cursory review of the draft reanalysis at best, leads to a less-than-desirable level of transparency and peer review, and undermines confidence in the process. Consequently, TCEQ is only able to provide preliminary comments based on a cursory review of the draft reanalysis.

If EPA seeks detailed and meaningful public input and technical comments, at a minimum EPA should: (1) extend the comment period at least 90 days past the August 19 deadline to allow stakeholders to perform a more detailed review of the volumes of relevant information and to comment on problematic issues associated with the draft reanalysis; (2) reschedule the SAB panel meeting to 90 days past the original dates of July 13-15; and (3) similarly extend the July 7 deadline for submitting comments for SAB consideration prior to the panel meeting.

Toxicology-Based Comments:

The complexity of the dose-response analyses of dioxin toxicity (cancer and non-cancer) and the potential for significant implications associated with the SFo (1E+06 per mg/kg/day) and RfD (7E-10 mg/kg-day) provided in the draft reanalysis indicate that EPA should allow a longer comment period for stakeholders to prepare more detailed comments. The allotted 90 days to prepare comments (August 19, 2010 deadline): (1) does not provide for an appropriate level of technical peer review for a draft 1,850-page document which represents years of work (e.g., dose-response analyses); (2) undermines confidence in the analyses and cited SFo and RfD values; and (3) calls into question the transparency of the TCDD toxicity factor development process as a thorough scientific review during this time frame is essentially unfeasible. Requiring comments be submitted by July 7, 2010, to be considered by SAB prior to the SAB panel meeting exacerbates the already significantly inadequate review time. Consistent with the inadequate review time allotted by EPA, extremely limited general toxicology-based comments are provided below.

Extrapolation Approach for the Carcinogenic Assessment

EPA has chosen to use a linear, low-dose extrapolation method for cancer effects as opposed to a nonlinear extrapolation method as recommended by NAS. EPA should adopt a nonlinear approach per the NAS committee, who unanimously agreed that the current weight of scientific evidence on the carcinogenicity of TCDD is adequate to justify the use of nonlinear extrapolation methods. TCEQ concurs with the NAS that scientific evidence (e.g., mode of action, tumor dose-response data) is adequate to favor the use of a nonlinear model that would include a threshold response over the use of the default linear

assumption. This determination is based on several lines of evidence, including: (1) available data suggest that TCDD (and other dioxins and dioxin-like compounds) are not

directly genotoxic, and there is general consensus in the scientific community that nongenotoxic carcinogens exhibit nonlinear dose-response relationships and thresholds (doses below which the expected response would be zero) are likely to be present; (2) there is widespread agreement in the scientific community that all or nearly all the adverse effects of TCDD (and other dioxins and dioxin-like compounds) depend on a receptor-mediated mechanism, acting through a mechanism involving the Ah receptor, and Ah receptor activation is a phenomenon that would be likely to cause the dose-response relationship to be sublinear at low doses (indeed, EPA has determined in previous evaluations of receptor-mediated carcinogens (e.g., numerous pesticides) that a nonlinear, low-dose model that may accommodate a threshold is appropriate); and (3) there is evidence of nonlinearity in various dose-response relationships for TCDD-induced tumors. In regard to (3) above, evidence of substantial hepatoxicity and a sublinear dose-response relationship in tumor-bearing female rats suggests that linear low-dose extrapolation is inappropriate. Additionally, for two types of epithelial tumors (keratinizing epithelioma of the lung and squamous cell tumors of the oral mucosal epithelium) the shape of the dose-response relationship suggests that they may be nonlinear. Also, the recent National Toxicology Program bioassay data (NTP 2004) are more consistent with a sublinear response that approaches zero at low doses rather than a linear dose response. Such evidence supports a nonlinear, low-dose extrapolation method as more justified and appropriate than the linear, low-dose extrapolation method used by EPA. However, contrary to the NAS and this evidence, EPA concludes that there is insufficient evidence to support a nonlinear approach. EPA should adopt a nonlinear approach per the NAS recommendation as the weight of scientific evidence supports it.

Additionally, EPA chose to use a 95% upper confidence limit (95%UCL) over the statistical best estimate of the regression coefficient. If EPA elects not to follow the NAS recommendation for a nonlinear approach, TCEQ suggests use of a SFo based on the best estimate of the regression coefficient as opposed to the 95%UCL. Based on Table 5-4 of the draft reanalysis, a SFo of around 5E+05 per mg/kg/day is preferred over use of the 95%UCL SFo as it is based on the statistical best estimate of the regression coefficient. This human study-based SFo is very similar to and supported by the SFo based on the well-conducted NTP (2006) rat study (Table ES-2), the most comprehensive evaluation of TCDD chronic rodent toxicity to date. Based on a very cursory review of the 1,850-page draft document, it does not appear to address, much less justify, use of a 95%UCL over the statistical best estimate of the regression coefficient.

Intrahuman Uncertainty Factor

EPA should give further consideration to justifying the reduction of the intrahuman uncertainty factor (UF_H) from 3 to 1 as the critical effects observed in the co-principal studies used to derive the RfD were found in sensitive subpopulations (children, neonates). There is historical precedent for EPA using a UF_H of 1 when the RfD is based on data in sensitive subpopulations such as infants and children (e.g., nitrate, nitrite, fluorine/soluble fluoride). Using a UF_H of 3 as in the draft reanalysis results in an RfD that may be

interpreted by the public to mean that based on average U.S. dietary intake (ATSDR 1998), which exceeds the draft RfD, TCDD-induced health effects such as increased thyroid stimulating hormone in neonates are likely occurring in the general population on a widespread basis.

Implementation-Based Comments:

Again, EPA must consider providing adequate review time for a critical examination of the bases of the SFo and RfD because these values have significant consequences for issues such as food safety, the federal drinking water maximum contaminant level (MCL) and surface water quality standards, and preliminary remediation goals (PRGs) applicable to dioxin (and other dioxin-like compounds) in soils at Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA/Federal Superfund) and Resource Conservation and Recovery Act (RCRA/Federal Hazardous Waste) corrective action sites. Consistent with the inadequate review time allotted by EPA, extremely limited general implementation-based comments are provided below.

Food Safety

TCEQ questions the risk assessment utility of an RfD value that is within or below the range of reported average dietary intake. The average intake from meat and eggs alone exceeds the RfD (ATSDR 1998). This draft RfD inevitably would raise public concerns about the safety of the U.S. food supply, especially given that the public frequently interprets the exceedance of a regulatory value as equivalent to an expectation of the occurrence of adverse health effects. A margin of exposure approach appears more appropriate than an RfD to evaluate the potential for non-cancer effects. The SFo provided in the draft reassessment also raises concerns about food safety given that risk from average dietary intake is above the acceptable excess risk range (1E-06 to 1E-04) established by EPA. Analyses such as these, using the RfD and SFo from the draft reanalysis, would imply that the U.S. diet results in TCDD hazard and risk that are considered unsafe and unacceptable from a regulatory perspective. Use of unjustifiably conservative toxicity factors for a chemical (or class of chemicals) may unnecessarily alarm the public and result in at least two negative responses: diluting the message of any future government risk warnings or diverting focus, funding, and resources from chemicals which realistically represent more of a public health hazard.

Surface Soil PRGs

The SFo given in the draft reanalysis (1E+06 per mg/kg/day) is 6.4 times higher than that used for the interim preliminary PRGs (1.56E+05 per mg/kg/day; EPA 2009), so revised cancer-based PRGs could be a factor of 6.4 times lower. The new RfD (7E-10 mg/kg-day) is 30% lower than that used for the interim preliminary PRGs (1E-9 mg/kg-day; EPA 2009), so revised non-cancer-based PRGs could decrease by 30%. Although the interim preliminary PRGs were ultimately based on non-cancer PRGs (EPA 2009), the greater conservativeness of the SFo given in the draft reanalysis may cause cancer-based PRGs to be the critical final PRGs. If protective at the 1E-05 excess risk level (similar to the interim preliminary PRGs in EPA 2009), the residential and commercial/industrial worker surface

soil PRGs could be over 150 times lower than the current PRGs (1 ppb for residential; 5 ppb for commercial/industrial (lower end of the range); EPA 1998), with the final residential PRG possibly being within the range of rural background concentrations (EPA 2009). EPA should reconsider finalizing a SFo which may result in setting a final residential PRG within background concentrations because such a PRG would not be feasible from a compliance perspective and could result in costly studies to determine site-specific background concentrations.

In regard to individual excess lifetime cancer risk (IELCR), EPA states on their website (http://www.epa.gov/oust/rbdm/sctrlsgw.htm), "The IELCR represents the incremental (over background) probability of an exposed individual's getting cancer (i.e., a risk occurring in excess of or above and beyond other risks for cancer such as diet, smoking, heredity). Cleanup standards calculated on the basis of excess risk limits correspond to allowable levels *in excess of the background concentrations of the chemicals of concern normally present in the source media*" (emphasis added). Since regulatory agencies are concerned with regulating *excess risk* (i.e., risk over natural background), technically, the risk due to naturally-occurring background soil levels should be excluded from comparisons to the EPA acceptable risk range. In other words, as EPA and other regulatory agencies are concerned with regulating excess risk over background, background TCDD levels (dioxin/furan TEQ) should be excluded from comparison to the TCDD PRG. Only levels *in excess of background concentrations* should be compared to TCDD PRGs since per EPA, "cleanup standards calculated on the basis of excess risk limits correspond to allowable levels *in excess of the background concentrations.*" Alternatively but based on the same considerations and with the same effect, the applicable soil PRG could be added to a representative background concentration for a site to derive a comparison value that represents a regulatory acceptable level of excess risk (i.e., risk over background). Since EPA is concerned with regulating excess risk over background, EPA should simply acknowledge that no action is necessary when TCDD levels (dioxin/furan TEQ) are within background at a remediation site, even if levels are above the applicable PRG.

Federal Drinking Water MCL and Surface Water Quality Standards

The SFo given in the draft reanalysis also has implications for the federal MCL for TCDD. Using the current SFo (1.56E+05 per mg/kg/day), risk associated with drinking water ingestion at the MCL is at the high end of the risk range deemed acceptable by EPA (≈ 1E-04). Use of the draft reanalysis SFo would result in the MCL being associated with a risk (≈ 9E-04) significantly higher than the upper end of the EPA acceptable risk range. The new RfD also has significant implications for the MCL. As the relative source contribution factor in the MCL calculation would likely be no greater than 1% (i.e., over 99% of exposure comes primarily from food), for a hazard quotient of 1 the current MCL would likely have to be reduced by over a factor of 100. Derivation of the most scientifically-defensible SFo and RfD values possible is also imperative due to the potentially significant impacts on surface water quality standards.

Recommendation:

Again, if EPA seeks thorough, detailed, and meaningful input and technical comments from the public and external experts on the EPA analyses conducted, at a minimum EPA should:

(1) extend the comment period at least 90 days past the August 19 deadline to allow stakeholders to perform a more detailed review of the volumes of relevant information and to comment on problematic issues associated with the draft reanalysis;

(2) reschedule the SAB panel meeting to 90 days past the original dates of July 13-15; and

(3) similarly extend the July 7 deadline for submitting comments for SAB consideration prior to the panel meeting. If EPA chooses not to provide additional time, EPA should carefully consider the broader consequences of finalizing the draft SFo and RfD values currently proposed, which could result in additional burdensome and costly regulation without meaningful protection of public health.

References:

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National Toxicology Program (NTP). 2004. Toxicology and Carcinogenesis Studies of 2,3,7,8-Tetrachlorodibenzo-p-dioxin (TCDD) (CAS No. 1746-01-6) in Female Harlan Sprague-Dawley Rats (Gavage Study). NIH Publication No. 044455. NTP TR 521. National Toxicology Program, Public Health Service, National Institutes of Health, Research Triangle Park, NC.

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