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05/05/2003 04:16:14 PM

Record Type: Record

To: Lorraine D. Hunt OIRA BC RPT/OMB/EOP@EOP

cc: David_Fischer@americanchemistry.com, jessica_stuart@americanchemistry.com
Subject: Comments on the Draft Report to Congress on the Costs and Benefits of Federal Regulation

Ms. Hunt:

I have attached the Chlorine Chemistry Council's comments on the Draft Report to Congress on the Costs and Benefits of Federal Regulation. Please feel free to contact me if you have any difficulty accessing the attachments or require additional information. A hard copy of our comments is in the mail as well. Thank you for your attention to this matter.

David Fischer
Managing Counsel

(See attached file: Appendix B.TIF)

(See attached file: Final TEF Comments on Letterhead as Appendix C.DOC)

(See attached file: cover letter.doc)

(See attached file: OMB comments on precaution.doc)

(See attached file: Appendix A.PDF)

- Appendix B.TIF
- Final TEF Comments on Letterhead as Appendix C.DOC
- cover letter.doc
- OMB comments on precaution.doc
- Appendix A.PDF

Appendix B

July 7, 2000

William H Farland, Ph.D.
8601D
USEPA Headquarters
Ariel Rios Building
1200 Pennsylvania Avenue, N. W.
Washington, DC 20460

Dear Dr. Farland,

Both of the signatories to this letter were members of the writing team for Chapter 8. We are writing here to express our concerns about Part 3 of the new dioxin reassessment. While Chapter 8 is significantly improved compared to earlier versions, Part 3 fails to adequately reflect the weight-of-the evidence interpretation of various mechanistic hypotheses discussed in Chapter 8 for the full characterization of dose-response.

We are particularly concerned with the presentation of the estimate of human lifetime cancer risk from dioxin exposure of 1 in 100. Without sufficient emphasis on the range of possible dose-response behaviors as discussed in Chapter 8, including nonlinear behaviors that would lead to considerably different estimates of risk, the presentation on a single risk estimate is misleading. In our opinion, the failure of the Agency to consider alternative dose response approaches is a key deficiency in Part 3. This single estimate based on linear risk models will generate a level of concern in the public, private, and regulatory sectors that is not consistent with a balanced interpretation the data on dioxin dose-response.

We do not dispute the conclusion that combining conservative assumptions about exposure with linear low dose behavior leads to the estimate of about 1 in 100. However, Chapter 8 also describes peer-reviewed, biologically plausible, nonlinear dose-response models for dioxin that provide good fits to dose-response data for enzyme induction and liver tumor promotion (Andersen et al., 1997; Conolly and Andersen, 1997). We believe that the data available on liver tumor promotion and regional enzyme induction strongly support non-linear relationships for enzyme induction and liver cancer. For us this is not just a plausible alternative, but also a preferred hypothesis with extensive experimental support. While our analyses have not included numerical estimates of cancer risk for dioxin, they provide a consistent interpretation of a large body of data in support on dose-response nonlinearity.

Some of the epidemiological datasets described in Chapter 8 can also be described with nonlinear models. However, none of the epidemiology data sets by themselves provide evidence proving linear or non-linear low dose behavior. Empirical analyses of dose response relationships indicated that the more complex endpoints were more likely to show non-linear behaviors. Thus, the weight of evidence does not provide unequivocal evidence supporting any single low dose behavior of dioxin. When linear and nonlinear models provide good descriptions of the data, they should both inform the weight-of-evidence evaluation of the mode of action and receive due emphasis in Part 3. If such an approach were followed, Part 3 would

include an upper bound risk estimate (i.e., 1 in 100) and a much fuller discussion of a nonlinear risk model with its implication for cancer and non-cancer risk assessments for TCDD.

The spirit of the proposed US EPA carcinogen assessment guidelines (1996) included evaluation of all plausible modes of action. If a single dominant hypothesis were heavily supported and others lacked firm support, the single dominant hypothesis would receive the main emphasis in the dose response assessment. This approach was pursued in the ILSI Panel's activities with chloroform (Andersen et al., 2000). However, when several modes of action with different implications for the dose response curve in the region of observation are consistent with the data, risk estimates should be derived from all of these proposed modes of action to inform risk management activities. This more even-handed approach to evaluating the larger body of data was not followed in Part 3.

We strongly recommend that a more inclusive approach be taken in presentation of these dose-response alternatives in Part 3. Data based risk assessments, like this one for dioxin, provide the opportunity to discuss the biologically plausible spectrum of risks that are consistent with the data. This flexibility is an enormous advantage over default-based assessments where little or no data are available to support consideration of a variety of plausible risks, nor of how risk may be distributed across the population as a function of exposure level. The dioxin dose response assessment should take full advantage of this flexibility to craft a balanced presentation in the face of the mechanistic uncertainties with this important environmental contaminant. Such a balanced presentation is currently lacking in Part 3.

Sincerely yours,

Rory B. Conolly, Sc.D., D.A.B.T.
Senior Scientist
Chemical Industry Institute of Toxicology
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Research Triangle Park, NC 27709

Melvin E. Andersen, Ph.D., D.A.B.T., C.I.H.
Professor, Department of Environmental Health
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We strongly recommend that a more inclusive approach be taken in presentation of these dose-response alternatives in Part 3. Data based risk assessments, like this one for dioxin, provide the opportunity to discuss the biologically plausible spectrum of risks that are consistent with the data. This flexibility is an enormous advantage over default-based assessments where little or no data are available to support consideration of a variety of plausible risks, nor of how risk may be distributed across the population as a function of exposure level. The dioxin dose response assessment should take full advantage of this flexibility to craft a balanced presentation in the face of the mechanistic uncertainties with this important environmental contaminant. Such a balanced presentation is currently lacking in Part 3.

Sincerely yours,

Rory B. Conolly, Sc.D., D.A.B.T.
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February 5, 2003

Dr. Andrew G. Salmon
Chief, Air Toxicology and Risk Assessment Unit
Office of Environmental Health Hazard Assessment
1515 Clay St., 16th Floor
Oakland, CA 94612

Re: Comments of the Chlorine Chemistry Council on OEHHA's Proposal to Adopt the World Health Organization's Toxicity Equivalency Factor Scheme

Dear Dr. Salmon:

The Chlorine Chemistry Council (CCC) appreciates this opportunity to comment on the California Environmental Protection Agency's Office of Environmental Health Hazard Assessment's (OEHHA's) *Proposal for the Adoption of the Revised Toxicity Equivalency Factor (TEF_{WHO-97}) Scheme* (OEHHA's Proposal). CCC, a business council of the American Chemistry Council, is dedicated to addressing public policy issues affecting the chlorine industry. Because OEHHA's Proposal has the potential to affect the chlorine industry by changing the method by which risk assessments for dioxins and related compounds are conducted, CCC has a strong interest in the Proposal.

I. Executive Summary

Inherent limitations exist in the WHO TEF scheme that make it inappropriate for use in assessing risks to exposures of dioxins and related compounds. In light of those limitations, CCC provides the following recommendations regarding OEHHA's Proposal to move from the I-TEF scheme to the WHO TEF scheme.

- OEHHA should not adopt the WHO TEF scheme for application in assessing risks to exposures of dioxins and related compounds because the scheme relies on numerous assumptions, thereby creating significant uncertainty.

Appendix C

- If OEHHA adopts the WHO TEF scheme in spite of its limitations, OEHHA should not apply the TEFs to co-planar PCBs.
    - OEHHA should quantify the uncertainty for each dioxin and furan TEF so that it is apparent in any risk assessment that relies upon TEF methodology.
    - OEHHA should embrace WHO's TDI for dioxin and its underlying conclusion that dioxin is a threshold carcinogen.
- OEHHA's Proposal provides insufficient procedures in violation of California's APA.
- OEHHA must clarify how the TEFs will be updated.

II. Introduction

The California Office of Environmental Health Hazard Assessment (OEHHA) has proposed to modify the method by which it calculates toxicity for dioxin-like compounds for purposes of its risk assessments for dioxins and related compounds under the California Toxic Air Contaminants Program. OEHHA is proposing to change from its current system that utilizes the International Toxicity Equivalency Factor (I-TEF) scheme to using the revised World Health Organization (WHO) - European Center for Environmental Health TEF scheme to facilitate the risk assessment of dioxins and dioxin-like compounds, including PCBs. Assigning TEF values to co-planar PCBs marks a distinct difference between the I-TEF scheme and the more recent WHO TEF scheme, and may greatly affect the assessment of risk posed by both dioxins and PCBs, as well as the risk management activities undertaken for those substances.

CCC believes there are a number of problems inherent to the WHO TEF scheme. These comments outline a number of those problems and address specific issues as they pertain to the OEHHA proposal and the application of TEFs to dioxins and dioxin-like compounds. In addition, CCC supports the comments of the American Chemistry Council – Polychlorinated Biphenyls Panel (ACC PCB Panel) on several points as discussed throughout these comments.

III. The inherent limitations in the WHO TEF scheme make it an inappropriate approach to assess risks posed by dioxins and related compounds.

CCC recognizes the value of using TEFs for dioxins and furans in limited circumstances. However, sweeping assumptions inherent in the TEF methodology render it inappropriate for predicting human health outcomes of dioxins, furans, and co-planar PCBs, particularly at background levels of exposure. Although OEHHA is currently using the I-TEF scheme, which is based on numerous compounded assumptions, the WHO TEF scheme would incorporate additional assumptions into dioxin risk assessments, creating even greater uncertainty. Significant additional assumptions and significant additional uncertainty results from the inclusion of PCBs to the WHO TEF scheme.

The TEF scheme is appropriate for purposes such as estimating releases for inclusion in EPA's Toxics Release Inventory (TRI). The TRI program can rely on estimated quantifications for the dioxin compounds without altering the effectiveness of the program or its goals. OEHHA, however, proposes to use the WHO TEF approach for conducting risk assessments, which requires far more precise calculations since even slight variations in a risk assessment can have far reaching implications. Not only might OEHHA's Proposal lead to poor public health decisions, but it will likely lead to other unnecessary societal costs such as increased clean-up costs and other misallocation of limited resources. The Agency for Toxic Substances and Disease Registry (ATSDR) has recognized the impact scientific uncertainties of the TEF approach can have on public health policies. Indeed, use of the TEF approach along with scientific uncertainty factors, fractional exposure from different pathways, and body burdens in the absence of exposure data are cited by ATSDR as the four scientific assumptions having the greatest impact on the development and use of public health policies for dioxin and dioxin-like compounds (Pohl *et al*, 2002).

The inherent limitations of the WHO TEF scheme, as discussed below, are the problems ATSDR referred to as greatly impacting public health policies for dioxins. TEFs likely differ for different endpoints, doses, species, and types of mixtures. Yet the TEF scheme relies on many assumptions, namely that each compound assigned a TEF elicits the same toxic endpoint - both cancer and non-cancer, that dose-response curves are parallel, and that the toxicities of these compounds are additive, regardless of the mixture. Further, the TEF scheme fails to consider the impact of naturally occurring Ah receptor agonists and antagonists.

A. <u>The WHO TEF scheme relies on the incorrect assumption that noncancer risks can be used to predict cancer risks.</u>

The WHO TEF scheme relies on the incorrect assumption that all congeners assigned a TEF value are carcinogenic agents and that the TEFs will accurately predict that carcinogenicity. CCC agrees with comments of the ACC PCB Panel, which pointed out that TEFs are based on a number of different endpoints, most of which are not related to carcinogenic activity. The use of relative non-cancer toxicities to predict cancer risks will incorrectly predict, both qualitatively and quantitatively, the cancer risks posed by most dioxin-like substances. PCBs provide an excellent example of over prediction. Co-planer PCBs are included in the WHO TEF scheme because they share some structural and toxicokinetic similarities to TCDD, and not because of carcinogenic activity. The carcinogenicity and toxicity of PCBs have been extensively examined and assessed. It is appropriate to use that relevant information rather than some convoluted, surrogate measure of PCB toxicity, such as dioxin TEFs.

B. <u>The WHO TEF scheme incorrectly assumes that all substances within the scheme possess parallel dose-response curves.</u>

The WHO TEF approach assumes that the dose-response curves for the PCDD/Fs and PCB congeners within the scheme are parallel to that of TCDD. Because TEFs are used to

equate the toxicity of PCBs and other congeners to TCDD at any dose or concentration, both the shape of the dose-response curve and the maximum response must be the same for the PCBs and other congeners and for TCDD. If this were not true, TEFs would not remain constant over a range of doses. In other words, TEFs would vary with dose, thereby invalidating the TEF scheme, which assigns a single value for each congener.

The basic assumption underlying the TEF scheme, that congeners and TCDD have parallel dose-responses, is incorrect. A number of studies have reported non-parallel dose-response curves for TCDD and dioxin-like PCB congeners (Kennedy *et al*., 1996; Safe, 1990). For instance, in a study of the effects of *in utero* exposure to two PCB compounds on the development of the male rat reproductive system, Faqi *et al*. (1998) found that neither PCB 77 nor PCB 126 produced the same spectrum of effects as those reported due to TCDD exposure at TEF-equivalent doses. Some similar responses were seen, but some key responses were absent, and other non-TCDD-like responses were observed. Furthermore, such parallelism of dose-response across end points and Ah receptor ligands does not occur, even among the simplest and best-understood responses such as hepatic enzyme induction (Walker *et al*., 1999).

C. <u>The WHO TEF scheme is based on the incorrect assumption that doses are additive for mixtures containing dioxins, furans, or co-planar PCB congeners.</u>

TEF schemes are based on the assumption that the doses of dioxin, dioxin-like congeners and PCBs are additive, i.e., that the toxicity of the mixture can be derived by adding the doses (modified through the application of TEFs) of TCDD and dioxin-like substances. Dose additivity can only occur when substances have the same mechanism of action. Using a less stringent standard for dose additivity, EPA assumes that substances share a common mechanism of action or a "common mechanism of toxicity" when they "share major steps leading to an adverse health effect following interaction of a substance with biological targets" (EPA, 1999; 2000).

Additivity in PCDD and PCB mixtures, however, has not been demonstrated across congeners and endpoints in animal studies (Harper *et al*., 1995; Safe, 1990; Starr, 1997). The applicability of additivity of dose response among humans is even less certain. In fact little has been done to elucidate the mechanism of action, or even the mode of action, for dioxin and dioxin-like substances. It is unwarranted, then, to assume that the toxicity of such mixtures can be predicted by summing the TEFs for the individual congeners.

The only mechanistic similarity EPA relies on to support an additive approach is Ah receptor binding. The adverse effects caused by chemicals that bind with the Ah receptor, however, can have a beneficial effect, an adverse effect, or no effect at all. A chemical that binds to the Ah receptor and causes any effect is termed an agonist. Conversely, a chemical that binds but has no effect or otherwise inhibits the occurrence of an effect is called an antagonist. Chemicals that bind to a receptor with no adverse effect - antagonists - compete with agonists for sites on receptors. Thus, while an antagonist occupies the receptor site, an agonist does not occupy it and therefore has no effect.

While the Ah receptor is capable of binding with a variety of molecules, the configuration of a chemical molecule determines whether binding occurs, as well as the strength of that bind. Should a chemical bind weakly to the Ah receptor it may be displaced by a competing chemical capable of creating a stronger bond with that receptor. Ah receptor binding, then, may be as competitive as it is additive.

D. The WHO TEF scheme is based on the incorrect assumption that interspecies differences in toxicity are inconsequential.

The WHO TEF scheme, like the I-TEF scheme, does not allow for variability of dose-response sensitivity between dissimilar species. For instance, TEF schemes assume that the level of enzyme induction reported in animal studies is equivalent to the level of induction that occurs in exposed humans. The responses observed in animal studies, then, are assumed to be predictive of human responses. A number of studies, however, suggest substantial differences between experimental animal and human responses (Brunner *et al*., 1996; Pohjanvirta *et al*., 1995; Safe, 1990; Zeiger *et al*., 2001).

Since carcinogenic responses are rarely consistent even among genders and strains of the same species it is unlikely that any single TEF value can adequately characterize the multiplicity and variability of toxicologically significant findings that have been reported in different species and target organs without an associated estimate of uncertainty (Starr *et al*., 1997). Further, it is doubtful that these responses can reliably predict human carcinogenic responses.

E. The WHO TEF scheme ignores important mechanistic uncertainties.

Sufficient mechanistic information is required to relate carcinogenic responses observed in experimental animals to human cancers. Although a few mechanistic responses have been identified in animals, it is unknown whether and to what extent any of those responses play a role in animal or human carcinogenicity. It is therefore improper to assume that humans will respond like experimental animals. The primary mechanistic event used to relate animal studies to potential human responses is the similarity in Ah receptor binding. Indeed, that molecular event underlies the TEF methodology. That methodology not only presumes that binding to the receptor is sufficient to cause cancer in animals, but also that the Ah receptor operates identically in animals and humans (Brief, 2001).

Such a broad assumption fails, however, for several reasons. First, very little is known about how dioxin ultimately causes cancer in animals and even less is known about how dioxin exposure might adversely affect humans. Second, it appears that the Ah receptor may exhibit species-specific differences. As previously stated, numerous studies have reported variations in dose-response sensitivities between and even among species. It is also unclear whether the Ah receptor is the same in animals and humans.[1] For instance, several studies have shown TCDD

[1] There are several different forms of the Ah receptor in mice alone, and it is known that the receptor differs between species. ATSDR states that "[t]he extent to which these forms [of Ah receptor] in mice and humans affect the types of responses elicited and the sensitivity to TCDD is unknown." ATSDR Profile at 233.

binding affinities of human Ah receptors to be much lower (as much as 10-fold) than those of rodent Ah receptors. Molecular genetics surely play an important role in explaining these differences. There is also evidence that suggests that Ah receptor variants are present in humans.

While it is clear that dioxin carcinogenicity may be determined by numerous biological and biochemical steps that occur after receptor binding, the actual mechanism for dioxin carcinogenicity has not been adequately characterized. The Ah receptor is a common receptor protein, and binding appears to be an early response to dioxin exposure in both animals and humans. Yet this means only that dioxin attaches preferentially to certain locations in cells. It does not directly imply a causal relationship between dioxin and cancer (Brief, 2001). Since it is not clear what role receptor binding plays in dioxin's carcinogenicity or whether receptor binding is even necessary to cause cancer, OEHHA's proposal is fundamentally flawed by relying on this mechanism as an indication of carcinogenicity.

F. <u>The WHO TEF approach neglects to consider the effect of naturally occurring Ah receptor binding compounds.</u>

In addition to PCDD/Fs, PCBs, and other anthropogenic chemicals, humans are exposed to hundreds of naturally-occurring compounds with Ah receptor agonist and/or antagonistic activity at dietary doses (Connor and Finley, 2003). These compounds, which exist in a wide variety of foods, including vegetables, fruits, dairy products, and cooked meats, exhibit many properties typically associated with dioxin and dioxin-like compounds, and can elicit Ah receptor-related responses following ordinary dietary doses (Safe, 1998). These endodioxins include certain indole carbinols and their derivatives, heterocyclic aromatic amines, tryptophan derivatives, cartenoids (Denison *et al*., 1998). Many of these compounds can be found in foods at concentrations thousands to millions of times greater than the trace levels of PCDD/Fs that may be present (Connor and Finley, 2003).

Since naturally-occurring dioxins may be present in the diet at relatively high concentrations, some researchers advocate that risk assessments of dietary toxic equivalents of dioxin and related compounds include these Ah receptor-active compounds. High TEQ doses of naturally-occurring compounds might suggest that the contribution by PCDD/Fs may be of little consequence and a lesser health concern. Likewise, high doses of naturally-occurring PCDD/F antagonists might suggest that any potential effects exerted by dietary PCDD/Fs would be inhibited (Finley *et al*., 2001).

IV. Application of the WHO TEF scheme to co-planar PCBs compounds the scheme's use of assumptions and creates greater uncertainty.

CCC concurs with the comments of the ACC PCB Panel that application of the TEF methodology is inappropriate for co-planar PCBs. The fallacy of the underlying assumptions inherent in the WHO TEF scheme is perhaps best demonstrated within the context of co-planar PCBs. Aside from applying the inherent problems of the TEF approach, using this approach to assess the risks of PCBs ignores a multitude of human epidemiological studies showing that

PCBs do not cause cancer in humans. The TEF approach as applied to PCBs simply does not fit the empirical reality of the large number of PCB-specific human cancer mortality and cancer incidence studies performed over past decades.

As the OEHHA proposal states, "the major difference between the new TEF table and the previous one is the inclusion of coplanar PCBs as compounds with dioxin-like activity." The TEF approach results in a supposed PCB cancer risk that may be up to 30 times greater than that based on observed effects in animals. Not only does this approach ignore EPA's 1996 PCB Cancer Reassessment, but it also excludes new information developed since the Reassessment. More overtly, it selects for animal data over human data. The inclusion of "dioxin-like" PCBs essentially disregards EPA policies for conducting a thorough review of the scientific literature before changing a chemical's carcinogenicity.

OEHHA's proposed use of the WHO TEF scheme for assessing the carcinogenic risks of PCBs is not scientifically supportable and will lead to inappropriate public health decisions. As proposed, the TEF approach could result in an order of magnitude increase in the predicted carcinogenicity rate for PCBs and dioxins. The societal costs of using the WHO TEF scheme could be great. For example, the monetary impact of assessing PCBs using the WHO TEF scheme could conceivably reach billions of dollars of expenditures to re-open and/or clean up a number of sites and stir unwarranted public concern about health risks. Pending a proper, thorough review of PCB carcinogenicity, OEHHA should continue to rely on PCB-specific cancer-dose-response studies.

V. OEHHA's Proposal violates California's APA.

CCC agrees with the comments submitted by the ACC PCB Panel that OEHHA's 30 day review and comment period for the Proposal is insufficient under the California Administrative Procedure Act, Cal. Gov. Code §11340 *et seq*. Although OEHHA classifies its change from the I-TEF to the WHO TEF scheme as "guidance", CCC agrees with the ACC PCB Panel's comments that the effect of reclassifying co-planar PCBs as dioxin-like compounds actually qualifies as a regulation. In proposing its regulation, OEHHA failed to comply with the procedures mandated by California APA. Finally, regardless of OEHHA's classification or its proposed action, the Agency failed to adequately describe the effects of its action.

VI. CCC's recommendations concerning OEHHA's Proposal.

At a minimum, OEHHA should not apply TEFs to co-planar PCBs. OEHHA should not assume toxic equivalency between dioxins and PCBs. Instead it should use PCB-specific data when conducting risk assessments of PCB mixtures.

Furthermore, OEHHA should quantify the uncertainty for the dioxin and furan TEFs so that the uncertainty is apparent in any risk assessment that relies upon TEF methodology. ATSDR recognizes the implications of applying multiple uncertainties to a dioxin risk assessment. "In practice, there is a big cost difference in trying to clean up a hazardous waste

site so that the final residue of dioxins is at the 10 ppb, 1 ppb, or 0.1 ppb level. Risk assessment is not a precise science, and different clean-up levels may be driven by or considered by the public as artifacts of the application of uncertainty factors. Because of the limited budget for environmental clean-up, overprotection at one site may result in lack of funds for another site where the resources are needed. For every environmental pollutant, health risks, clean-up benefits, and economical feasibility must be carefully evaluated." (Pohl *et al*., 2002). Basing a risk assessment on TEF values derived using a multitude of uncertainties and unproven assumptions can greatly alter the standards to which a site must be cleaned.

Additionally, if OEHHA is intent on using the WHO TEF scheme, OEHHA should also embrace WHO's recent reassessment of its TDI of 1 to 4 TEQ/kg bw/day for dioxin and its underlying conclusion that dioxin is a threshold carcinogen. (WHO, 1998)

Finally, OEHHA should clarify how the TEFs will be updated. Although OEHHA recognizes in its proposal WHO's suggestion to reevaluate the TEFs every five years, OEHHA also admits that a "timetable for completion of the next review process has not been defined" in spite of the WHO TEFs being developed six years ago. Because WHO is not reviewing its TEFs in a timely fashion, OEHHA should identify a specific mechanism to routinely evaluate the TEF values, based on evolving science. Since TEFs are reassessed by the international community only sporadically, it is necessary that OEHHA specify a plan to routinely evaluate the specific TEF values on a regular, predetermined basis to consider new scientific data.

VII. Conclusion

Based on the inherent limitations in the WHO TEF scheme, CCC recommends that OEHHA not adopt this scheme for application in assessing risks from exposure to dioxin and dioxin-like compounds. Furthermore, if OEHHA insists on adopting the WHO TEF scheme, OEHHA should not apply the scheme to co-planar PCBs. OEHHA should also quantify the uncertainty for each dioxin and furan TEF so that it is apparent in any risk assessment that relies upon TEF methodology. If OEHHA is intent on using the WHO TEF scheme, OEHHA should also embrace WHO's TDI for dioxin and its underlying conclusion that dioxin is a threshold carcinogen. Finally, OEHHA should clarify how the TEFs will be updated to include new scientific data.

Please direct any questions or comments you may have concerning this submission to Todd Abel (703-741-5856) or Jessica Stuart (703-741-5419).

Sincerely,

Clifford T. "Kip" Howlett, Jr.
Executive Director,
American Chemistry Council,
Vice President

VIII. References

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CHLORINE CHEMISTRY COUNCIL

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May 5, 2003

Lorraine Hunt
Office of Information and Regulatory Affairs
Office of Management and Budget
NEOB, Room 10202
725 17th Street, NW
Washington, D.C. 20503

Re: Comments on OMB's Draft Report to Congress on the Costs and Benefits of Federal Regulation (68 Fed. Reg. 5492, Feb 3, 2003).

Dear Ms. Hunt:

The Chlorine Chemistry Council (CCC) is pleased to provide the *Interagency Work Group on Risk Management* with the following examples in which EPA embeds "precaution" in current risk assessment procedures through the use of conservative assumptions. Importantly, conservative assumptions can have dramatic impacts on risk management decision-making. The CCC is a business council of the American Chemistry Council and has a keen interest in federal risk assessment procedures, particularly as they impact chlorine chemistry.

As discussed in the accompanying comments, EPA's draft dioxin reassessment serves as a vivid example of EPA's reliance on conservative assumptions. As such, EPA fails to comport with its own Risk Characterization Handbook, the centralized body of risk characterization implementation guidance for Agency risk assessors. In particular, EPA's reliance on conservative assumptions is both unreasonable and inconsistent with the worldwide convergence on a dioxin health assessment value of 1 to 4 pg/kg/day. Further, EPA fails to provide a risk management and public health context for its dioxin risk characterization. Consequently, neither risk managers nor the public are able to determine the public health implications of EPA's reliance on these conservative assumptions.

The so-called Stage 2 Disinfectants and Disinfection Byproducts Rule (Stage 2 Rule) serves as another example of EPA's embedding precaution into risk assessment procedures. Unfortunately, EPA has not adequately conveyed this uncertainty, or the precautionary nature of the Stage 2 Rule. Numerous statements in its prepublication draft overstate the link between DBP exposure and potential reproductive and developmental risks. The *Interagency Work Group on Risk Management* should carefully consider how EPA addresses highly uncertain, non-quantifiable benefits in the proposed Stage 2 Rule. In affect, EPA grossly overstates the risk benefits of the rule by failing to acknowledge the evident uncertainties surrounding the risks of DBP exposure.

CCC appreciates this opportunity to provide these comments to OMB and the *Interagency Work Group on Risk Management*. Should you require additional information, feel free to contact David Fischer at (703) 741-5179.

Sincerely,

Clifford T. "Kip" Howlett, Jr.
Executive Director,
American Chemistry Council,
Vice President

Enclosure

Comments of the Chlorine Chemistry Council on OMB's

Draft Report to Congress on the Costs and Benefits of Federal Regulation

68 Fed. Reg. 5492
Feb 3, 2003

Submitted
May 5, 2003

WAYS IN WHICH PRECAUTION IS EMBEDDED IN CURRENT RISK ASSESSMENT PROCEDURES

The Chlorine Chemistry Council is pleased to provide the *Interagency Work Group on Risk Management* with the following examples in which EPA embeds "precaution" in current risk assessment procedures through the use of conservative assumptions. Importantly, conservative assumptions can have dramatic impacts on risk management decision-making. As noted recently by the Agency for Toxic Substances and Disease Registry, in the context of hazardous waste sites,

> Risk assessment is not a precise science, and different clean-up levels may be driven by or considered by the public as artifacts of the application of uncertainty factors. Because of the limited budget for environmental clean-up, overprotection at one site may result in lack of funds for another site where the resources are needed. For every environmental pollutant, health risks, clean-up benefits, and economical feasibility must be carefully evaluated.[1]

I. EPA's Reliance on Conservative Assumptions in the Draft Dioxin Reassessment

EPA's current Draft Dioxin Reassessment provides numerous examples of the precautious nature of the Agency's risk assessments, especially in light of principles laid out in EPA's own Risk Characterization Handbook. As stated in EPA's Risk Characterization Handbook (Guidance), the centralized body of risk characterization implementation guidance for Agency risk assessors, "effective characterization depends on transparency, clarity, consistency and reasonableness (TCCR)."[2] Yet, EPA's draft dioxin reassessment fails significantly to comply with this Guidance. In particular, EPA's reliance on conservative assumptions yields a risk characterization that is demonstrably unreasonable and inconsistent. Further, EPA fails to provide a risk management and public health context for its dioxin risk characterization. Consequently, neither risk managers nor the public are able to determine the public health implications of EPA's reliance on these conservative assumptions.

The Guidance is based on the recommendations of several other reports that emphasize the importance of providing a risk management and public health context in which to characterize risks. These reports include The Presidential/Congressional Commission on Risk Assessment and Risk Management's *Framework for Environmental Health Risk Management*[3]

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[1] Pohl, HR, *et al.*, *Public Health Perspectives on Dioxin Risks: Two Decades of Evaluations*, Hum. Ecol. Risk Assess. 8(2):233-250 (2002) (*see* Appendix A).

[2] Environmental Protection Agency, Science Policy Council, Risk Characterization Handbook at 1 (Dec. 2000).

[3] The Presidential/Congressional Commission on Risk Assessment and Risk Management, *The Framework for Environmental Health Risk Management* (1997) [hereinafter Commission *Framework*]. The 1990 Clean Air Act Amendments mandated The Presidential/Congressional Commission on Risk Assessment and Risk Management to develop the Framework, which lays out a six-step process for risk management. The Framework integrates risk management into the risk assessment process, stating, "The nature, extent, and focus of a risk assessment should be

and the National Research Council's report on *Understanding Risk: Informing Decisions in a Democratic Society*[4].

Significantly, the Guidance is referenced in EPA's Information Quality Guidelines as an example of "the numerous systems and practices in place that address the quality, objectivity, utility, and integrity of the information."[5] These Guidelines are meant to ensure and maximize the quality of information disseminated by the Agency. Thus, EPA must implement the Risk Characterization Handbook and its TCCR principles to comply with these Guidelines.

A. EPA's Reliance on a Conservative Linear Model to Quantify Dioxin Cancer Risks

EPA relies solely on a conservative linear default model to quantify dioxin cancer risks. This approach differs from other world bodies (e.g., the European Commission Scientific Committee on Foods (EC), the Joint FAO/WHO Expert Committee on Food Additives (JECFA)) that have determined that a threshold model is more consistent with the science concerning dioxin's carcinogenic action. These determinations are based on the weight of the evidence that dioxin is a nongenotoxic carcinogen. In addition, the Agency for Toxic Substances and Disease Registry (ATSDR) has concluded that "USEPA's model of the dose response for cancer is inconsistent with the recommendations of the President's Committee on Risk Assessment and Management for cancers thought to be elicited by nongenotoxic mechanisms (CRARM 1996)."[6] Moreover, as noted in a recent GAO report, the threshold model is in stark contrast to EPA's non-threshold determination and conclusion that "the upper bound on the general population's lifetime risk for all cancers from dioxins might be on the order of 1 in 1,000 or more (i.e., people

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guided by the risk management goals." *Id*. at 23. Identification of the risk management goals is the first step in the process. Only after these goals are identified should the risk assessment be performed, putting the risks into context based on the goals already identified. An accurate risk characterization is based on both scientific information and the risk management goals. Ultimately, the characterization should include stakeholder opinions and social and cultural impacts.

[4] National Research Council, *Understanding Risk: Informing Decisions in a Democratic Society* (1997) [hereinafter *Understand Risk*]. A committee of the National Research Council (NRC) issued this report in response to the charge that the risk analysis process breaks down when the risk manager translates the risk assessment. To completely disassociate the framework from the traditionally distinct two-step process of risk assessment and risk management, the committee abandons use of the terms "risk assessment" and "risk management." The committee explicitly states, "We believe that acceptance of too strict a separation between risk assessment and risk management has contributed to an unworkably narrow view of risk characterization." *Id*. at 34. Instead, the committee describes risk characterization as a series of steps that incorporate both processes and refers to them as "analysis" and "deliberation." Chapter 5 of this book is dedicated entirely to integrating the two steps of risk characterization. According to the committee, "both analysis and deliberation are useful in every step leading to risk characterization, and participants in risk decisions are likely to be better informed if the two processes are combined in appropriate ways." *Id*. at 118.

[5] Environmental Protection Agency, Guidelines for Ensuring and Maximizing the Quality, Objectivity, Utility, and Integrity of Information Disseminated by the Environmental Protection Agency, at 10 (2002).

[6] Pohl, *supra* note 1, at 240 (*see* Appendix A).

might experience a 1 in 1,000 increased chance of developing cancer over their lifetime because of exposure to dioxins)."[7]

A threshold approach is also consistent with animal studies addressing carcinogenicity of dioxin. For example, in a recent review article by Dragan and Schrenk, the authors conclude that "While the mechanism of carcinogenicity induced by TCDD is unknown, the processes involved have a no-effect level…."[8] According to JECFA's dioxin risk assessment, humans would need to consume orders of magnitude more dioxin on a daily basis than current intakes to reach a comparable body burden observed in rats associated with a lowest observable effect level.

In addition, authors of the draft dioxin reassessment's dose-response chapter expressed concern that EPA's dioxin risk characterization failed to "adequately reflect the weight-of-evidence interpretation of various mechanistic hypotheses" related to dioxin carcinogenicity. Those authors stated that the data "strongly support non-linear relationships for enzyme induction and liver cancer. For us this is not just a plausible alternative, but also a preferred hypothesis with extensive experimental support."[9] This is consistent with a peer-review report of EPA's dioxin reassessment conducted by EPA's Science Advisory Board which concluded that the "majority of panel members have concerns about Agency cancer risk estimates associated with current population exposures and feel that it was not appropriate for the agency to characterize the risks in such a quantitative manner without providing a similar qualitative estimate of uncertainty."[10]

In sum, EPA's conservative cancer predictions are not in step with the conclusions of other federal and international bodies, and have been challenged by a number of EPA's peer reviewers and other scientists.[11] Indeed, in the view of a significant number of scientists, a threshold based cancer analysis is the scientifically preferred approach. Therefore, EPA's use of a conservative linear model portrays the Agency's further embedding of precaution in the dioxin risk assessment.

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[7] U.S. General Accounting Office, "Environmental Health Risks, Information on EPA's Draft Reassessment of Dioxins," GAO-02-515, at 31 (2002) [hereinafter GAO Report].

[8] Dragan and Schrenk, *Animal Studies Addressing the Carcinogenicity of TCDD (or Related Compounds) with an Emphasis on Tumor Promotion,* Food Additives and Contaminants, Vol. 7, No. 4, 289 (2000).

[9] Letter to William Farland from R. Conolly and M. Andersen, July 7, 2000 (*see* Appendix B).

[10] EPA Science Advisory Board, *Dioxin Reassessment: An SAB Review of the Office of Research and Development's Reassessment of Dioxin*, EPA-SAB-EC-01-006 at 6 (2001) [hereinafter SAB Report]. There was also a lack of consensus among the SAB Panel regarding the strength of weight of evidence for supporting the classification of TCDD as a human carcinogen and disagreement as to whether effects observed in the laboratory would be observed in humans at lower levels of exposure. Further, some SAB members did not consider it appropriate to apply the standard default assumptions recommended by EPA's cancer guidelines, and "particularly the use of a linear response model . . . ." *Id*. at 2.

[11] *See*, e.g., ISRTP Conference Proceedings, EPA's Characterization of Dioxin Risks: Do Background Dioxin Exposures Pose a Human Health Threat? (Oct. 6, 2000).

B. EPA's Reliance on Conservative Uncertainty Factors In Calculating a Theoretical Reference Dose

As noted above, there appears to be a worldwide convergence on a dioxin health assessment value of 1 to 4 pg/kg/day.[12] EPA has expressed the view that the EC and JECFA tolerable intake levels were practical risk management calculations, rather than true risk assessment derivations. We strongly disagree with that characterization. The risk assessments of these international bodies clearly derive protective dioxin exposure levels.

Notwithstanding EPA's views on the EC and JECFA tolerable intake levels, the ATSDR minimal risk level (MRL) of 1 pg/kg bw/day, which is for all intents and purposes equivalent to an RfD, would still be orders of magnitude higher than EPA's implied RfD.[13] As stated by GAO, "EPA's traditional approach for setting a reference dose gives more weight to scientific uncertainties…."[14]

ATSDR, on the other hand, has calculated far less conservative safety/uncertainty factors that are more consistent with the wealth of both animal and human dioxin data. For example, ATSDR concluded that humans were *not* more sensitive than the experimental species for which toxicity data exist, and that therefore the toxicodynamic portion of the default factor of 10 was set to 1. The conclusions detailed in the ATSDR MRL worksheet demonstrate that the database on dioxin is sufficiently robust to justify reducing the traditional default uncertainty factors used in calculating MRLs and RfDs.

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[12] Our recommendation that EPA more carefully consider the approaches of other federal and international bodies is consistent with SAB's comments. SAB stated,

> [s]ome Members think that EPA should provide more comment on the "minimal risk" levels promulgated by ATSDR and the World Health Organization (WHO). In 1995, the SAB Committee required a clear comparison to dioxin-related assessments by other agencies. EPA's response to this request (e.g., the terse treatment on p. 110 of Part III, lines 6-12) is not adequate, in the view of these Members. The document does not explain why ATSDR's "minimum risk" criterion would differ from EPA's unstated criterion. In the case of the WHO position, the document offers no explanation as to why EPA's position is different. No new analysis is necessarily required, but EPA does need to offer a clear explanation of why they are differing from the conclusions of other US and international agencies that have taken official positions on TCDD.

SAB Report, *supra* note 10, at 21.

[13] Environmental Protection Agency, SAB Review Draft, Exposure and Human Health Reassessment of 2,3,7,8- Tetrachlorodibenzo-*p*-Dioxin (TCDD) and Related Compounds (Sept. 2000), *available at* http://www.epa.gov/ncea/pdfs/dioxin/part3/chapter1-6.pdf. [hereinafter Draft Dioxin Reassessment] ("**Any RfD that the Agency would recommend under the traditional approach for setting an RfD is likely to be 2-3 orders of magnitude (100-1,000) below current background intakes and body burdens**." (*emphasis added*)).

[14] GAO Report, *supra* note 7, at 30.

C. EPA's Reliance on TEF/TEQ Methodology

The toxic equivalency (TEQ) approach accounts for the toxicities of the individual dioxin and dioxin-like compounds. Toxicities are assigned to individual compounds using a Toxic Equivalency Factor (TEF). TEFs represent order of magnitude estimates of the relative potency of dioxin-like compounds compared to 2,3,7,8-tetrachloro-p-dioxin (i.e., dioxin). The total toxicity of a given mixture of dioxin and dioxin-like compounds is determined by multiplying the TEF for each compound in the mixture by the concentration of the individual compound, and then summing these products. Sweeping assumptions inherent in the TEQ methodology render it inappropriate for predicting human health outcomes of dioxins, furans, and co-planar PCBs, particularly at background levels of exposure.

CCC recognizes the value of using the TEQ methodology for dioxins and furans in limited circumstances; for example, in estimating releases for inclusion in EPA's Toxics Release Inventory (TRI). The TRI program can rely on estimated quantifications for the dioxin compounds without altering the effectiveness of the program or its goals. EPA, however, relies on the WHO TEQ approach for conducting risk assessments, which requires far more precise calculations since even slight variations in a risk assessment can have far-reaching implications.

Specific TEFs likely differ for different endpoints, doses, species, and types of mixtures. Yet the TEQ approach relies on many assumptions, namely that each compound assigned a TEF elicits the same toxic endpoint for both cancer and non-cancer effects, that dose-response curves are parallel, and that the toxicities of these compounds are additive, regardless of the mixture. Further, the TEF scheme fails to consider the impact of naturally occurring Ah receptor agonists and antagonists.[15]

In its draft dioxin reassessment, EPA cites several studies in which the *in vivo* biological activity of mixtures are over-predicted, usually by factors of two to five, but dismisses this degree of over-prediction as insignificant[16]. Given EPA's judgment that current background exposures are at or near levels that produce effects in humans, a factor of two to five over-prediction by the TEQ scheme, observed consistently in studies of effects of interest due to exposure to mixtures, is significant.

D. The Dioxin Risk Characterization Has No Risk Management Or Public Health Context

The dioxin risk characterization lacks a risk management context and, as a result, it is likely to lead to a great deal of confusion as to its public health implications. In the absence of a risk management context provided by EPA, such contexts will be supplied by stakeholders, who

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[15] CCC's describes more fully the conservative nature of the TEF methodology in comments on the California Environmental Protection Agency's Office of Environmental Health Hazard Assessment's *Proposal for the Adoption of the Revised Toxicity Equivalency Factor (TEF_{WHO-97}) Scheme* (Feb. 5, 2003) (*see* Appendix C).

[16] Environmental Protection Agency, SAB Review Draft Part II, Chapter 9 of the Draft Dioxin Reassessment: Toxic Equivalency Factors (TEFs), 9-20 (Sept. 2000) *available at* http://www.epa.gov/ncea/pdfs/dioxin/part2/drich9.pdf.

are likely either to misunderstand or to misuse the conclusions. Dioxin is, after all, only one of a great many substances that would be relevant to any particular risk management situation and the potential health effects of dioxin are only one possible risk management concern.

The National Academy of Sciences' *Red Book*[17] and *Science and Judgment in Risk Assessment*[18] define risk characterization as the final step in health risk assessment. According to those reports, the goal of risk characterization is to provide an understanding of the type and magnitude of an adverse effect that a particular chemical or emission could cause under particular circumstances. *Science and Judgment* goes further than the *Red Book*, however, by acknowledging the role of the risk manager: "The results of the risk characterization are then communicated to the risk manager with an overall assessment of the quality of the information in the analysis….The risk manager then makes decisions on the basis of the public-health impact as determined by the risk characterization and other criteria outlined in the appropriate statute."[19] A risk characterization thus needs to convey information that can be used in decision-making.

More recently, the National Academy of Sciences report *Understanding Risk* criticized the earlier definitions of risk characterization as "seriously deficient," while recognizing that those definitions are the prevailing view at EPA and other agencies. *Understanding Risk* concluded instead that "[r]isk characterization should not be an activity added at the end of risk analysis…[but] should be a *decision-driven activity*, directed toward informing choices and solving problems"[20]. Furthermore, "The purpose of risk characterization is to enhance practical understanding and to illuminate practical choices."[21] In other words, risk characterization does not work as a stand-alone activity and must be performed as part of a risk management decision-making process.

In 1997, the Commission on Risk Assessment and Risk Management proposed a Framework for Environmental Health Risk Management Decision-Making based on the belief that risk assessments should be performed within a risk management context.[22] The Commission concluded that risk characterization should be guided by the need to address a risk management problem and should form a common basis for the understanding of a problem among stakeholders.

Without a risk management context for the dioxin risk characterization, its relevance and its message are very difficult to assess. As *Understanding Risk* puts it, "It is not sufficient to get the science right; an informed [risk management] decision also requires getting the right science,

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17 National Research Council, *Risk Assessment in the Federal Government: Managing the Process* (1983)

18 National Research Council, *Science and Judgment in Risk Assessment* (1994).

19 *Id*. at 68.

20 *Understanding Risk, supra* note 4, at 2 (*emphasis added*).

21 *Id*. at 16.

22 Commission *Framework*, *supra* note 3.

that is, directing the scientific effort to the issues most pertinent to the decision."[23] A carefully prepared summary of scientific information will not give the participants in a risk decision the understanding they need if that information is not relevant to the decision to be made. Determining the public health implications of the present dioxin risk characterization is not possible in the absence of a risk management context, or in the absence of knowing what the risk management problem is that EPA is trying to solve.

The dioxin risk assessment lacks a public health context. Without a public health context, the importance of dioxin related to other public health threats is unknown, leading potentially to misdirected risk management resources.

Science and Judgment in Risk Assessment describes the job of the risk manager as being responsible for making risk management decisions "on the basis of the public health impact" or a risk, among other things. To do so, a risk characterization must be communicated in a way such that the risk manager knows what the public health impact of the exposure of concern actually is. The dioxin risk assessment does not identify the public health problem that it is trying to solve; instead, it starts with an exposure and then tries to find something wrong with it. Elucidating the public health problem is particularly critical in the context of dioxin, since dioxin sources may be natural, anthropogenic, or reservoir-based and may or may not contribute to actual human exposure.

Many factors are known to contribute to morbidity and mortality; the public health community has not identified dioxin as one of those factors. Environmental exposures are thought to contribute to a relatively small percentage of morbidity and mortality although presumably we experience many kinds of environmental exposures. If our dioxin exposures are lower now than they have been in 30 years and are continuing to decrease, in the context of all the other exposures and other known contributors to morbidity and mortality that we experience, it just does not seem plausible that dioxin is a leading threat to public health. If EPA believes that dioxin is a leading threat to public health, which is the clear implication of the risk assessment, it must provide some factual *public health comparative* basis for that conclusion.

E. EPA's Dioxin Risk Characterization Summary Statement Fails to Convey the Uncertainties Embedded Within the Risk Assessment

The dioxin risk characterization summary statement is arguably the most important section of the voluminous draft dioxin reassessment.[24] It is the statement that will be widely read as representing the message of the dioxin characterization. Thus, at a minimum, the statement must provide a public health context that

- accurately reflects the risk assessment, and
- conveys useful information for risk management decision-making

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[23] *Understanding Risk, supra* note 4, at 16.

[24] Draft Dioxin Reassessment, *supra* note 13.

Regrettably, the dioxin risk characterization summary statement is confusing and inadequate as a stand-alone piece. It neither reflects the risk assessment nor conveys sufficient information about the assumptions and uncertainties that underlie the risk characterization.

In its current form, the summary statement is misleading and of little use to stakeholders and risk managers who would like to understand either the content or the implications of the risk assessment. The clear implication of the summary statement is that we are exposed to dioxin at levels that are causing a wide variety of diseases; exposure to dioxin is, therefore, a public health problem.

However, the summary does not describe *how* we are exposed to dioxin, or what we can do about it. A reader thus does not know what to avoid or how to reduce his or her risk. There is no uncertainty conveyed with regard to *whether* dioxin is a public health problem; at the same time, no convincing evidence is produced demonstrating that it is a problem. Given the tremendous uncertainty about dioxin's likely public health threat and the huge implications for risk management if the threat is as high as the risk characterization seems to say it is, greater clarification as to what is known and what is assumed regarding dioxin's impact on public health is needed.

II. EPA Fails to Adequately Convey the Uncertainty of the Stage 2 Disinfectants and Disinfection Byproducts Rule

The so-called Stage 2 Disinfectants and Disinfection Byproducts Rule (Stage 2 Rule)[25] serves as another example of EPA's embedding precaution into risk assessment procedures. In 2003, EPA anticipates proposing the Stage 2 Rule, which will address potential health risks from exposure to disinfection byproducts (DBPs). Stage 2 builds on the previously promulgated Stage 1 Rule, both of which were products of extensive multi-stakeholder negotiation through a negotiated rulemaking process.

Reproductive and developmental health risks have been a major topic of discussion throughout the negotiated rulemaking process. EPA and independent scientific reviewers have recognized, however, that an association between these risks and DBP exposure is uncertain, and that the data are insufficient to support a quantified risk assessment at this time.

Unfortunately, EPA has not adequately conveyed this uncertainty, or the precautionary nature of the Stage 2 Rule. Several statements in its prepublication draft overstate the link between DBP exposure and potential reproductive and developmental risks.

> *EPA believes the implementation of the Stage 2 DBPR will reduce peak and average levels of disinfection byproducts (DBPs) in drinking water supplies which will result in reduced risk from reproductive and developmental health effects and cancer.*[26]

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[25] Environmental Protection Agency, Proposed Rule, National Primary Drinking Water Regulations: Stage 2 Disinfectants and Disinfection Byproducts Rule (Stage 2 DBPR), 40 C.F.R. §§ 9, 141, 142 (proposed Oct. 17, 2001), *available at* http://www.epa.gov/safewater/mdbp/st2dis-preamble.pdf.

[26] *Id*. at 1 (*emphasis added*).

These changes in compliance determination and sampling plans will moderate exposure inequities across the distribution system which will provide benefits from reduced health risks.[27]

EPA believes that the proposed Stage 2 DBPR will decrease risk to pregnant women and their fetuses.[28]

These statements imply that a causal relationship exists between DBP exposure and reproductive and developmental risks, and that the rule will reduce such risks.

This overly precautionary discussion may be carried forward into the Agency's economic analysis of the Stage 2 rule. For example, the Agency may seek to bolster the estimated benefits of the rule by including a quantitative estimate or a "sensitivity analysis" of benefits related to reproductive and developmental risk reductions. Any such estimate would be based on scientifically unsupportable assumptions (e.g., how many miscarriages might be attributed to DBP exposure, and how many might be avoided by the rule). Such an approach would raise significant data quality concerns. Furthermore, speculative estimates of reproductive risks would likely cause unwarranted alarm about the safety of public water supplies. Even if EPA does not use such statements to bolster the rule's presumed benefits, these statements may prompt water utilities to engage in unwarranted deselection of disinfectants.

The Interagency Work Group on Risk Management should carefully consider how EPA addresses highly uncertain, non-quantifiable benefits in the proposed Stage 2 Rule. In affect, EPA grossly overstates the risk benefits of the rule by failing to acknowledge the evident uncertainties surrounding the risks of DBP exposure.

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[27] *Id*. at 44 (*emphasis added*).

[28] *Id*. at 52 (*emphasis added*).