To: John Bell[jbell@hsia.org]; tom.d.blackman@lmco.com[tom.d.blackman@lmco.com]; Shanna.clark@us.af.mil[Shanna.clark@us.af.mil]; Bernard Gadagbui[gadagbui@tera.org]; Lynne Haber[haber@tera.org]; Joseph.Haney@tceq.texas.gov[Joseph.Haney@tceq.texas.gov]; troy.j.meyer@honeywell.com[troy.j.meyer@honeywell.com]; john.lowe@ch2m.com[john.lowe@ch2m.com]; LiuSh@cdmsmith.com[LiuSh@cdmsmith.com]; Morningstar, Mary P[mary.p.morningstar@lmco.com]; Mumtaz, Moiz (ATSDR/DTHHS/ETB)[mgm4@cdc.gov]; Ed Pfau[epfau@hullinc.com]; David Reynolds[dreynolds@iwpnews.com]; Lorenz Rhomberg[lrhomberg@gradientcorp.com]; rodbthompson@comcast.net[rodbthompson@comcast.net]; gdt1@cdc.gov[gdt1@cdc.gov]
Cc: Flowers, Lynn[Flowers.Lynn@epa.gov]; Bussard, David[Bussard.David@epa.gov]; Benson, Bob[Benson.Bob@epa.gov]; Griffin, Susan[Griffin.Susan@epa.gov]; Vu, Chau[Vu.Chau@epa.gov]; Sivak, Michael[Sivak.Michael@epa.gov]; Hubbard, Jennifer[Hubbard.Jennifer@epa.gov]; Johnson, Jeremy[Johnson.Jeremy@epa.gov]; Bailey, Marcia[bailey.marcia@epa.gov]; McDonough, Margaret[Mcdonough.Margaret@epa.gov]; Olsen, Marian[Olsen.Marian@epa.gov]; Adams, Glenn[Adams.Glenn@epa.gov]; Podowski, Andrew[Podowski.Andrew@epa.gov]; Khoury, Ghassan[Khoury.Ghassan@epa.gov]; CNorman@PattonBoggs.com[CNorman@PattonBoggs.com]; Virginia J CIV NAVFAC SW Makale[virginia.makale@navy.mil]; audrey.rush@epa.state.oh.us[audrey.rush@epa.state.oh.us]; kroner@tera.org[kroner@tera.org]; Ooi, Sim[SOoi@pb.com.au]; janusz.byczkowski@epa.state.oh.us[janusz.byczkowski@epa.state.oh.us]; roger.brewer@doh.hawaii.gov[roger.brewer@doh.hawaii.gov]; John DeSesso[Jdesesso@exponent.com]; Pottenger, Lynn[lpottenger@dow.com]; Becker, Rick[Rick_Becker@americanchemistry.com]; Kimberly_Wise@americanchemistry.com[Kimberly_Wise@americanchemistry.com]; ANDERSON, JANET K GS-13 USAF DoD AFCEE/TDV[janet.anderson.5@us.af.mil]; LiuSh@cdmsmith.com[LiuSh@cdmsmith.com]; Clark, Becki[Clark.Becki@epa.gov]; Chiu, Wuehsueh[Chiu.Weihsueh@epa.gov]; Jarman, Ruth[Rjarman@pb.com.au]; Stralka, Daniel[Stralka.Daniel@epa.gov]
From: Michael Dourson
Sent: Tue 2/12/2013 10:31:40 PM
Subject: Re: 6th Conference Call regarding Alliance for Risk Assessment Project on TCE
MAIL_RECEIVED: Tue 2/12/2013 10:32:42 PM
Cardiac development in various species.doc
TCE RfC Imprecision and IA Variability.doc
WOE TCE Developmental ARA.doc
Hazard Ranges of the TCE RfCs.docx

Dear Colleagues

Please find attachments for this Thursday's conference call, February 14th, at 10 am (Washington, D.C. time). We anticipate a longer than usual call due to the extent of the work on which we wish your collective feedback. The call in number is 424 203-8400, code: 833440#.

A draft agenda follows:

- Ground rules for participation (5 minutes, Dourson)
- Introductions and individual group reasons for participation (10 minutes, all)
- Review of work done to date (60 minutes, Thompson, Pfau, Gadagbui, Dourson, Rhomberg, Todd, Lowe)
    - Cardiac development in various species;
    - TCE RfC imprecision and IA Variability;
    - WOE TCE developmental ARA;
    - Hazard Ranges of the TCE RfCs;
- Building the coalition (10 minutes, all)
- Good and welfare (5 minutes, all)

The “TCE RfC Impression and IA Variability” paper has been divided into four sections: Imprecision in the RfC; Imprecision in the Hazard estimate based on the RfC; Variability in Indoor Air Concentrations; and Accounting for Variability in Indoor Air Concentrations with respect to the 21-day time window.

As before, the floor will be open for questions from observers and comments and suggestions for improvement from participants. Please feel free to invite any interested party to attend.

Cheers!

Michael Dourson
Chair, Steering Committee
Alliance for Risk Assessment (*ARA*)

On 1/10/13 8:04 PM, "Michael Dourson" <mdourson@tera.org> wrote:

Dear Colleagues

Thanks for taking time out of your busy schedule this week to discuss this project. A draft set of notes follows; please feel to add to these notes.

Sincerely,

Michael Dourson
Chair, Steering Committee
Alliance for Risk Assessment (*ARA*)

Notes of the 5th Conference call on the TCE ARA Project: 1-8-13

Present:

- John Bell, Halogenated Solvents Industry Alliance (observer)
- Tom Blackman, Lockheed Martin (observer)
- Shanna Clark, USAF (observer)
- Michael Dourson, Alliance for Risk Assessment (participant)
- Bernard Gadagbui, Toxicology Excellence for Risk Assessment (participant)
- Lynne Haber, Society of Toxicology’s Ethical, Legal, and Social Issues Specialty Section (observer)
- Kip Heaney, Texas Commission on Environmental Quality (observer)
- Troy Kennedy, Honeywell (participant)
- John Lowe, CH2M Hill (participant)

- Charlene Lu, CDM Smith (observer)
- Mary Morningstar, Lockheed Martin (observer)
- Moiz Mumtaz, Agency for Toxic Substances and Disease Registry (observer)
- Edward Pfau, Hull and Associates (participant)
- Dave Reynolds, Inside Washington News (observer)
- Lorenz Rhomberg, Gradient (participant)
- Rod Thompson, Alliance for Site Closures (participant)

The meeting started with a discussion of ground rules for participation by Mike Dourson. Discussion topics are completely open and reportable. However, with the exception of expected reports, attribution of a statement or question during discussion to either a person or his/her organization is not permitted. Observers are allowed to ask questions, but otherwise not participate in the discussion. Afterwards, all folks introduced themselves and gave reasons for participation or observation.

A review of additional work since the time of the last conference call then followed. Ed Pfau of Hull and Associates and Rod Thompson of the Alliance for Site Closures reported briefly about the imprecision of risk values in relationship to Hazard Quotient of 1, including the imprecision of RfCs ("with uncertainty spanning perhaps an order of magnitude") based on the underlying toxicity data and choice of uncertainty factors, and the imprecision of multiple exposure measurements and different averaging times. One participant brought up the idea of using the half life of a chemical as a way to choose an appropriate averaging time, for example, longer half lives would allow longer averaging times (and correspondingly smaller half lives would suggest smaller averaging times). Another participant brought up the idea of using the length of window of cardiac development in humans as a way to judge the averaging time, based in part of a meeting with EPA/NCEA scientists where this topic came up in relationship to the cardiac effects in rat fetuses. Ed Pfau and Rod Thompson agreed to work these considerations into their developing position.

Bernard Gadagbui of TERA then reported some progress on reviewing the risk assessment values of various organizations that could be brought into a risk management use (or not) of the critical effect of fetal heart malformations. He stated that a draft report will be developed by the time of the next conference call.

Mike Dourson of the *ARA* then reported on the preliminary results of two methods for the development of ranges of risk around and EPA's TCE RfCs. These methods were adapted from two case studies on another *ARA* project entitled "Beyond Science and Decisions: From Problem Formulation to Dose Response," both of these case studies were vetted by a senior risk assessment science panel (http://www.allianceforrisk.org/Workshop/Panel.htm). The first case study entitled, "Use of biomarkers in the benchmark dose method," has 4 approaches to estimating this risk. Dourson reported on the first, and simplest of these four. Preliminary results using EPA's TCE BMD/L suggested that risks above EPA's RfC for nephropathy were more severe than the results for fetal cardiac effects, but started at a higher dose. One participant queried whether the response in this case study truly reflected the human

risk to sensitive individuals or was it an alternate procedure to address exposures above the RfC. Dourson responded that the risk is intended to represented sensitive individuals, but that this risk is preliminary, since the other 3 approaches are each expected to be more accurate (and complicated). The purpose of exploring the first approach was to determine whether exploring these additional approaches would be fruitful. Preliminary results suggested that this exploration would be fruitful and that nephropathy might become the sentinel effect. Results from these additional approaches will be developed in the next several weeks.

The second case study was entitled "Estimating Risk Above the RfD Using Uncertainty Factor Distributions." The preliminary results of this study suggested that EPA's RfCs for nephropathy and immunotoxicity were the same at a 95% confidence level, whereas RfCs for fetal cardiac effects and immunotoxicity were not similar at any confidence level. Also, depending on a risk manager's choice of confidence level, different RfCs would result, either higher or lower than what might be stated on EPA's IRIS or elsewhere (http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?iter).

A brief discussion of building the coalition then followed. Two additional groups joined the coalition. These groups are: CH2M Hill with John Lowe as the contact, and Gradient Corporation with Lorenz Rhomberg as the contact. Both CH2M Hill and Gradient will be asked to nominate a scientist to the working group. Participating groups now include: Alliance for Site Closures, Alliance for Risk Assessment, CH2M Hill, Gradient, Honeywell, Hull and Associates, and Toxicology Excellence for Risk Assessment. As mentioned in previous emails, other groups are welcome to join the coalition by either endorsement, sweat equity, or cash donation (or a combination of these) at any time. Groups can also decide to drop out at any time.

Under good and welfare it was announced that Moiz Mumtaz of ATSDR is the Society of Toxicology's Lehman award winner for 2013. This annual and singular award is for for major contributions that improve the scientific basis of risk assessment. Dr. Mumtaz is well known for his work on chemical mixtures risk assessment.

The next conference call will be held in about 4 weeks time.

-----Related Notes-----
Options to accomplish the work:

1. Staff of one of the *ARA* nonprofit partners would look at relevant scientific data, summarize critical studies and choices of dose response assessment models, and prepare tables for easy reference by a science panel. The panel would then get together for a one or two day meeting to discuss these summarized data and models and to determine the appropriate RfDs. The panel would be selected by the Advisory Committee, or perhaps the Steering Committee of the *ARA*. A subsequent peer review of the panel's work might be useful for this option. This option would cost the most.
2. Staff of one of the *ARA* nonprofit partners would look at relevant scientific data,

summarize critical studies and choices of dose response assessment models, and determine the appropriate RfDs directly. A subsequent peer review of the partner's work would likely be useful for this option. This would cost less than the option 1.

3. **[This is the current option being used.] The Advisory Committee would designate one individual from each group who would work with other designated members to look at relevant scientific and management data, review critical studies and choices of dose response assessment models, and determine the appropriate risk management guidelines directly. A subsequent peer review of the group's work might be useful for this option. This would cost less than options 1 and 2.**

Relationship among groups:

- The Steering Committee of the Alliance for Risk Assessment (*ARA*) (http://www.allianceforrisk.org/ARA_Steering_Committee.htm) is like a board of directors for a nonprofit organization. The Steering Committee set the direction of the *ARA* and agrees to all incoming projects, but the committee does not do any work, although some of its member might. If the *ARA* was a separate nonprofit organization (it is not yet this), the Steering Committee would be considered its owners. This is true of any nonprofit organization in the US. For example, TERA is a nonprofit and its board of directors (http://www.tera.org/about/boardofdirectors.html) is considered to be the owner, even though none of the board members get paid and they do not own anything (if a nonprofit goes bankrupt, the board will distribute its assets to other nonprofit organizations).
- The Advisory Committee is simply the committee that leads any particular project. In contrast to the Steering Committee, all members of the Advisory Committee are active and supporting participants in the specific project. For example, the *ARA* project "Beyond Science and Decisions: From Problem Formulation to Dose Response" has 55 sponsors, 4 of which form the Advisory Committee (ACC, EPA, TCEQ, and TERA). The Advisory Committee has not yet formed for this project but this is getting closer; several members on the conference calls will likely be members of this committee.
- A Science Panel for a project may or may not be needed depending on the judgment of its Advisory Committee. Advise of the *ARA* Steering Committee is often helpful in this judgment and sometime it takes an active role in the panel's selection. For example, the Science Panel of the "Beyond Science and Decisions: From Problem Formulation to Dose Response" was chosen by the *ARA* Steering Committee, because the project's Advisory Committee wanted a neutral group making the selections.
- A peer review committee might also be needed for any particular project. This can be seen as a variation in the Science Panel, particularly when the project has a more limited time span.

In option one, the Science Panel does most of the technical work. The project's

Advisory Committee would likely either choose this panel, or it could ask the *ARA* Steering Committee to do this. If the latter, the Advisory Committee would be able to nominate folks to serve on this panel, including perhaps one or more members from its group. The project Advisory Committee would then take the role of support, such as procuring resources for the project and it could certainly participate in the public parts of the project. In option 2, one or more of the nonprofit partners do the technical work. Afterwards, the project's Advisory Committee could serve as a peer review, or it could select an independent group. **In option 3, the project's Advisory Committee would do the technical work. Afterward, it could have an independent panel review its work, or perhaps submit it to a journal for publication.**