



SCAPA
Chemical Exposure Working Group (CEWG)
Chemical Mixture Working Group (CMWG)

Highlights
CEWG/CMWG Annual Meeting
Tuesday, May 15, 2012, 5:00 p.m. PDT

Participants

Jayne-Anne Bond, ATL International	Vern McDougal, ATL International
Bud Bucci, Hanford	Mike O'Keeffe, NNSA (phone)
John Ciolek, AlphaTRAC, Inc.	Rocky Petrocchi, Petrocchi Associates
Doug Craig, ATL International	Joe Terranova, BNL
Dave Freshwater, NA-41	Richard Thomas, Intercet
Cliff Glantz, PNNL	Tom Tuccinardi, ATL International
Jonathan Lowrie, URS SMS SRS	Juan Yao, PNNL
Po-Yung Lu, ORNL	Xiao-Ying Yu, PNNL
Ray Lux, Lux Consulting	

Roll Call

Cliff Glantz conducted a roll call, acknowledged that 17 individuals representing six DOE/NNSA sites were present, and brought the CEWG/CMWG Meeting to order.

Discussion

CEWG Activities

Jayne-Anne Bond introduced herself as the new chair of the CEWG and thanked the outgoing chair, Doug Craig, for his many years of service. Fortunately, Doug will continue to support the activities of the CEWG.

Jayne-Anne announced that she and Tom Tuccinardi have drafted new and updated materials for the PAC/TEEL and CEWG web pages. Tom and Jayne-Anne are working on a new CEWG charter that will be provided in a link on the CEWG web pages. The purpose of the charter is to help CEWG members to understand its tasks and avoid conflicts with other EMI SIG working groups (e.g., the Chemical Screening Working Group).

Jayne-Anne reiterated that substantial changes have been made in the TEEL development methodology and that this updated methodology was used to derive the PAC values presented in PAC/TEEL Revision 27. This represents the most extensive reconfiguration of the TEEL methodology since its inception in the 1990s. Approximately 80% of TEEL values presented in the PAC/TEEL data set have changed. Jayne-Anne indicated that she does not want to review all of the major changes. Doug Craig's presentation during the SCAPA meeting summarizes these changes (http://orise.orau.gov/emi/annual-meeting/2012/Presentations/SCAPA_CraigBondLu.pdf).

Further changes to the TEEL development methodology are presently being discussed. These changes will not appear until the release of PAC/TEEL Revision 28, which is tentatively scheduled for release in early 2013.

It is noted that TEEL values were derived for a few chemicals using an “unapproved” route of entry (i.e., route of administration) or an unapproved laboratory animal. These exceptions were made because these were the only data available for this chemical. Is this appropriate? The following three questions were posed:

1. Should a TEEL be established for these types of chemicals?
2. Would it be better to use a Structure Activity Relationship (SAR) for these chemicals?
3. If such a chemical is a solid, should a starting point of 10 mg/m³ be used for the derivation of TEELs?

These questions will be tackled by the TEEL development team before the release of PAC/TEEL Revision 28.

The topic of subcutaneous tumor formation was raised, and it was pointed out that almost any substance can cause tumor formation if administered subcutaneously for a long exposure period. This is especially true for most solids. Some laboratory tests involve a one-year exposure to the material. Accordingly, a question was posed as to whether the data from such studies are appropriate for TEEL development purposes with its focus on emergency preparedness and response. The consensus of the working group appeared to be that these data were not appropriate for TEEL development. Rocky Petrocchi mentioned that he prefers to use SARs rather than data such as obtained from subcutaneous exposure studies. Rocky believes that this is better than using insoluble or poorly soluble particles not otherwise specified. Doug reminded us that the latter is only for solids and non-volatile liquids, which, in general, should be non-toxic.

NA-41 reminded that if the default TEEL development methodology does not hold together, it is the assignment of the TEEL Review Committee to review and assign TEEL values for individual outlier chemicals.

Jayne-Anne reviewed the concept of removing non-harmful chemicals from the PAC data set; candidates for removal from the PAC data set are provided through a link on the PAC home page. This link, http://www.atlntl.com/DOE/teels/teel/Candidate_materials_for_removal_for_publishing_final.xls, opens up an Excel spreadsheet providing the names, Chemical Abstract Service Registry Numbers, and chemical descriptions of 114 chemicals that are candidates for removal from the PAC data set; representing a little over 3% of the chemicals in the PAC data set.

Joe Terranova asked if a confidence level can be placed on a PAC value. Perhaps this could be done by color-coding PAC values based on various particular confidence level bins. The reply was that this would make for a rather festive dataset and there is already a lot of information provided in the PAC data set. Jayne-Anne stated that she would be hesitant to provide confidence level information because of the difficulty involved in providing technical justification for confidence information. Dave Freshwater mentioned that we might consider something equivalent to the AEGLs holding status. This would involve releasing a preliminary PAC value, and not releasing a final PAC value unless there is sufficient confidence in doing so. This should be the subject of future discussions within the working group and TEEL development team.

Mike O'Keefe asked why TEELs are available for chemicals that cause cancer down the road and shouldn't the focus be on acute health effects. Historically, the initial impetus for the development of TEELs came from people working on documented safety analyses, and not from those focusing on emergency preparedness and emergency response. Dave reported that most requests for TEELs still come from people focusing on safety analyses and not emergency planning. TEELs are mentioned in Appendix B to DOE Standard 1189, Integration of Safety into the Design Basis.

Dave emphasized that the definition of TEELs is based on acute exposures; the TEELs are not concerned with chronic exposures. There is been some confusion about this, particularly in the Chemical Mixture Methodology (CMM), which has traditionally used chronic Health Code Numbers (HCNs). These chronic HCNs were intended to serve as surrogates for missing acute HCNs and not to inject the consideration of chronic effects into the CMM. The incidents of chronic health effects from an acute (i.e., short-term) exposure to a chemical are comparatively rare.

Doug Craig raised the issue of taking species out of the TEEL derivation process. Using exposures data from different species without weighting the results from different species doesn't make sense to him. This is particularly troublesome because some TEELs, particularly those based on TClo and other similar parameters are heavily dependent on the species involved in the study. Dave thought that the external review committee addressed this issue in its report. Dave will review the external review committee's recommendation to determine if, in revising the TEEL derivation methodology, we inadvertently worked away from something that needs consideration. There were several changes to the TEEL methodology that cause minor changes, but when taken together their cumulative effects can be significant.

Doug then asked whether we are discussing this in the appropriate venue, or if we should first put together a position paper. Doug decided that he will discuss these issues in more detail at the TEEL Advisory Group (TAG) meeting.

CMWG Activities

Xiao-Ying Yu introduced herself as the new chair of the CMWG and thanked the outgoing chair, Rocky Petrocchi, for his many years of service. Fortunately, Rocky will also continue to work as an active member of the CMWG and the Chemical Mixture Methodology (CMM) development team.

Xiao-Ying reported on the work of the CMM team over the past year. In summer 2011, interns were available to take a hard look at the CMM using 24 test mixtures. Their study showed that there were benefits from using the HCN-based approach in cases where more than one chemical was a significant contributor to the HI, and there was some difference in the HCNs between those significant chemicals. However, for some test mixtures there was a tendency towards over-conservatism; providing results equivalent to the over-conservative method of summing all the HIs for the chemicals in the mixture without regards to whether these health effects were additive.

Xiao-Ying indicated that acute health effects were the dominant driver in determining HI values in all of the test cases; HCNs associated with chronic health effects did not affect final results. It was debated whether to continue to consider using chronic HCNs because the definition of PAC-2 includes impaired ability to escape and irreversible or other serious, long-lasting, adverse health effects; and whether the latter, which is associated with the short-term exposures (i.e., ≤ 1 hour), can result in a chronic health effect.

To further study the CMM and to look for ways to enhance it, the interns explored how applying different weighting factors to the HCNs might affect results. They developed and tested several easy-to-implement candidate HCN weighting approaches. Some additional benefit was obtained from one of the tested approaches while still maintaining conservatism. However, it is still uncertain whether there is enough technical justification to apply a weighting factor approach.

In analyzing the CMM testing results, questions were raised about the use of "Mode of Action" categories. Rocky provided a brief review on where the HCN categories came from; there was a seminal article in Patty that introduced these categories. It was asked if there is a better measure of health effects. In response, the CMM team is currently considering an alternative approach that is largely based on Target Organ System Effects and drops many of the problematic Mode of Action categories. This will be discussed in more detail in a special meeting of the CMWG that will be held on Wednesday morning at 8:45.

Joe Terranova empathized that the aged and drug-exposed populations also need to be protected. Accordingly, TEELs and AEGLs need to take into consideration the compromised members of the population. It was commented that this is already accounted for in the PAC derivation process.



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Juan Yao, the newest intern, was introduced. She is planning to focus her Master's thesis on the topic of HCNs for nanoparticles—a very challenging topic.

Adjournment

The meeting was adjourned at 6:00 p.m. PDT. Cliff thanked everyone for their time and contributions.