Responses to Comments from Panel Members and the Public

Texas Commission on Environmental Quality

Responses to Peer Review Report

April 5, 2012
(Pages 35-39)

http://www.tceq.state.tx.us/assets/public/implementation/tox/peer_review/report_comments_&_responses.pdf

2.1.10

Is the approach for identifying Inhalation Effect Levels consistent with accepted risk assessment methodology (Section 3.14).

Reviewer 3

The approach described in section 3.14 for identifying inhalation no adverse effect levels is appropriate and consistent with current practices.

Response: No response required.

Reviewer 5

The approaches described in 3.14 are consistent with current practice.

Response: No response required.

Reviewer 6

There is no one standard risk assessment methodology, rather there are many accepted risk assessment methodologies adapted to each unique relevant scenario. TCEQ's selection of risk assessment methodology is well adapted, explained and appropriate for the applications described. Rating=3. As requested, to quantify relative strengths and weaknesses, I have used a positive 5 point system for relative strength (1 is very weak, 2 is weak, 3 is consistent with accepted practice and documentation, 4 is strong, 5 is very strong).

Response: No response required.

Reviewer 7

I thought this was an interesting discussion of predicting the central estimate of the lowest exposure that can be expected to cause an adverse response in humans. It does not include use of UFs, so is not what is usually done in risk assessment methodology. It is for informational purposes only (page 95, line 26) and for comparison with "safe" levels determined with the use of UFs for risk assessment. The general tone of this section reminds me of when I served on a committee to advise the Navy on the toxicity of airborne substances on submarines. The commanders of the submarines were not interested in "safe" levels for a general population. They wanted to know when they had to take emergency measures and surface to vent the air on the submarine. In that case, the population at risk was somewhat homogenous, i.e., they were healthy young men. But in Section 3.14, the general population is of concern, including among others the elderly, the young and the highly sensitive. So it is much harder to estimate a practical, "real" inhalation effects level for such a diverse group. There will be a great deal of uncertainty associated with such an estimate. There is a good discussion in this section about those uncertainties. But there is one paragraph (Section 3.14.2) in which the authors claim that their approach will allow them to predict an

inhalation effects level with "a reasonable degree of certainty" (page 96, line 24). Using duration adjustments and UFs is said to add uncertainty (page 96, lines 21-22). This gives a false impression of precision in the calculation of the inhalation effects levels that is not warranted. The effects level will depend on who is being exposed. It would be more reasonable to give a range of effects levels, considering the diverse population of concern. The approach is apparently intended to give a "central tendency" value, but this should not be confused with certainty. As long as these calculations are restricted to the DSDs and all the caveats that are discussed in Section 3.14 are clearly given, then I have no problem with the exercise. However, it must be made clear that such estimates have a great deal of uncertainty.

Response: TCEQ disagrees with this comment. TCEQ does not claim that the approach will always allow prediction of an inhalation effects level with "a reasonable degree of certainty," TCEQ merely states "a reasonable degree of certainty" as a desired goal or attribute and to the extent possible, attempts to identify procedures consistent with furthering the purpose of, "identifying a level where with a reasonable degree of certainty, a response in some individuals may be expected." Furthermore, TCEQ does not claim that a given level will, or can, account for any potential intrahuman variability in sensitivity beyond that captured by the dose-response data made basis for the value (i.e., the value cannot directly account for truly sensitive subpopulations, if any, if relevant human dose-response data are not available). Ultimately, the degree of certainty/uncertainty associated with the expectation of a human response occurring in some individuals will depend upon the data available. As acknowledged in the comment, the TCEQ provides a good discussion of the associated uncertainties. The TCEQ understands that effects levels may vary among individuals for a given chemical, and if the data allow, the TCEQ will provide a range of effects levels considering population diversity. If dose-response data are only available for a group that is in fact less sensitive, then any resulting effects level would be even more certain to increase the likelihood of an effect in a general population that includes more sensitive subgroups. The goal of the TCEQ is to reduce the uncertainty, to the extent possible, associated with the expectation of a human response occurring in some individuals at an air concentration based on the dose-response data available, which may not include the potentially most sensitive subpopulations.

However, when determining the lower end of actual effects levels, available data are a limiting factor. Consistent with the comment, the TCEQ will discuss the caveats and uncertainties associated with these values in the DSDs.

Reviewer 10

Typically this type of assessment is not done except sometimes when incidence levels are calculated for risk benefit determinations. Thus it is difficult to answer the question. Is this determination for susceptible populations? If so that should be stated.

Response: TCEQ is interested in this determination for the general population and susceptible populations in particular, as data allow.

Section 3.14.1 uses the most sensitive species. This may not always be appropriate. For irritants, the rat is probably the better model than the mouse. The most appropriate species should be used, not the most susceptible. You are using an HEC determination that has problems. See my general comment 5 on dosimetry corrections.

Response: Text has been added to this section regarding appropriate animal model considerations, and consistent with TCEQ procedures, the most defensible established dosimetric adjustments will be performed.

Section 3.14.2. Since you are not using UFs that implies the effects predicted will occur at lower doses in susceptible individual. If that is what is meant then state it.

Response: UFs are not used in this evaluation as they introduce uncertainty about the expectation of a human response occurring in some individuals based on the dose-response data. Not using UFs in-and-of itself does not imply that significant intrahuman variability exists regarding sensitivity to the critical effect for a given chemical, much less that effects will in fact occur at lower concentrations in some susceptible individuals. For example, in some cases, the dose-response data used may include susceptible individuals or populations such that the intrahuman UF would have been 1. No changes were made.

Section 3.14.3. There are a lot of caveats in this section so I am not sure what will be calculated. One gets the impression that the problems are so great these values might not be calculated. Consideration might be given to computing the 1 in 10 cancer rate. It would be a novel exercise of predicting cancer rates in the experimental range. If these calculations are performed TCEQ might consider staying away from predicting cancer from single exposures. The uncertainties with lifetime predictions are difficult enough without adding single exposure estimates.
Response: TCEQ will keep these considerations in mind.

Reviewer 12
This section attempts to apply what this reviewer refers to as probabilistic considerations of PODs (both N/LOAEL and BMD/Cs) and what they may mean in human populations. Most "accepted" risk assessment methodologies do not usually provide the reader with this aspect, thus this approach should be considered not only as acceptable, but an attribute of the guidance.

Response: This section was developed in response to public inquiries regarding likely effects levels. Along with the derived health-protective values (e.g., ReVs, ESLs), the TCEQ believes these levels will help provide the public with a more complete picture of the conservativeness inherent in the protection of public health and environmental quality in our heavily-industrialized state, and agrees that this additional approach is an attribute to TCEQ guidance.