January 14, 2002

Dear Dr. :

Enclosed please find the IRIS Summary Sheets and Toxicological Review for Xylenes. Included in this package are (1) the Work Assignment Authorization, which includes the charge questions for this review and (2) the xylenes reports. Also attached to this letter are two forms, the conflict of interest statement and the confidentiality agreement form. Please read and sign these forms and fax them within the next week to Valerie Schwartz of Versar at 703-642-6954.

The technical charge for the review is provided in the enclosed Work Assignment Authorization. Please provide your comments in the following format:

- General Impressions

  Provide overall impressions of document (approximately 1-2 paragraphs in length).

- Response to Charge Questions

  Provide responses to each of the charge questions (the charge questions are in the attached WAA).

- Specific Observations

  Provide specific observations, mentioning page and paragraph number.

- Recommendations

  Please identify your overall recommendation, based on your reading and analysis of the information provided.

We request that you complete your review by **February 14, 2002**. Please e-mail your review, as an MS Word attachment, to me at bottimoredavid@aol.com If you have any questions, please call me at (305) 898-5257.

Sincerely,

David Bottimore
Program Manager

**WORK ASSIGNMENT AUTHORIZATION**

| | |
|---|---|
| **WORK ASSIGNMENT #:** | Task Order 61 |
| **TITLE:** | Scientific Peer Review of the Draft Documents IRIS Summary and Toxicological Review for Xylenes |
| **CONSULTANT NAME:** | |
| **VERSAR JOB NUMBER:** | 4902.061 |
| **PERIOD OF PERFORMANCE:** | Completion of peer review by February 14, 2002 |
| **FIXED PRICE:** | Not to exceed (NTE) |

## Background

EPA generates a number of scientific documents with regulatory and informational applications. Among the most visible of the informational products are the Summaries and Toxicological Reviews produced for the Integrated Risk Information System (IRIS). As a means of ensuring a high quality science in its products, the Agency has instituted a rigorous peer review process. Through this process the chemical manager who produces the document submits the assessment to experts both internally and outside of the Agency to critique the document. Because of the visibility and the range of uses of IRIS assessments it is essential that the EPA scientists and outside experts, through the external review, evaluate the accuracy of the content and quality of judgement used in this assessment.

The Toxicological Review and IRIS Summary for Xylenes has been prepared jointly by contractors and the EPA chemical manager. They have been reviewed internally by EPA scientists. Comments made by the EPA reviewers have been considered and, where deemed appropriate, incorporated into the document. The next step in the peer review process is to obtain independent review by national experts in toxicology and related fields.

## Work Scope and Charge

The primary function of the peer reviewer should be to judge whether the choice, use, and interpretation of data employed in the derivation of the assessments is appropriate and scientifically sound. This review is not of the recommended Agency risk assessment guidelines or methodologies used to derive cancer or RfD/C assessments as these have been reviewed by external scientific peers, the public, and EPA Science Advisory Boards. The reviewer's comments on the application of these guidelines/methodologies within the individual assessments is, however, welcomed and encouraged. For example, the reviewer may ascertain whether or not there is data sufficient to support use of other than default assumptions for areas such as sensitive subpopulations or linear cancer extrapolation. The reviewer may also have opinions on other areas of uncertainty such as subchronic to chronic duration (when only a subchronic study is available) or an incomplete data base but should focus on the specific area of uncertainty rather than on the magnitude of the overall estimate.

Please review the IRIS xylenes documents according to the following guidance and charge questions. Keep in mind that the RfD and RfC should reflect chronic exposures generally encountered under environmental conditions, as laid out in Section 1 of the Toxicological Review.

Your comments should address the overall quality of the documents and provide input to the Agency on approaches to improve the assessment from both technical and communication standpoints (e.g., clarity, conciseness, etc) and on the integration of data into an overall characterization of hazard. Comment on how well the data from individual studies are characterized and comment on the conclusions that are drawn from each study, and how well the data are integrated into an overall conclusion and characterization of the hazard as presented in sections 4.5, 4.6, 5 and 6.

In addition to commenting on these general issues, please respond to the following charge questions:

1. Are you aware of any other data/studies that are relevant (i.e., useful for the hazard identification or dose-response assessment) for the assessment of the adverse health effects, both cancer and noncancer, of this chemical?

2. For the RfD and RfC, has the most appropriate critical effect been chosen. Points relevant to this determination include whether or not the choice follows from the dose-response assessment, whether the effect is considered adverse, and if the effect and the species in which it is observed is a valid model for humans.

3. Have the *cancer and* noncancer assessments been based on the most appropriate studies? These studies should present the critical effect/cancer (tumors or appropriate precursor) in the clearest dose- response relationship. If not, what other study (or studies) should be chosen and why?

4. Studies included in the RfD and RfC under the heading "Supporting/Additional studies" are meant to lend scientific justification for the designation of critical effect by including any relevant pathogenesis in humans, any applicable mechanistic information, any evidence corroborative of the critical effect, or to establish the comprehensiveness of the data base with respect to various endpoints (such as reproductive/developmental toxicity studies). Should other studies be included under the "Supporting/Additional" category? Should some studies be removed? Do you agree with the selection of the NOAEL/LOAEL for determination of the RfD given the manner in which the data are reported?

5. For the noncancer assessments, are there other data that should be considered in developing the uncertainty factors or the modifying factor? Do you consider that the data support use of different (default) values than those proposed?

6. Do the confidence statements and weight-of-evidence statements present a clear rationale and accurately reflect the utility of the studies chosen, the relevancy of the effects to

humans, and the comprehensiveness of the data base? Do these statements make sufficiently apparent all the underlying assumptions and limitations of these assessments? If not, what needs to be added?

The review should consider the use of secondary data, uncertainty, and variability. The term "secondary data" is defined as the review or use of someone else's environmental or health data that was developed for a different purpose. This includes data used from citations, from the literature searches, from hard copies, and from computer data bases. While reviewing these documents, please give attention to EPA's use, analysis, and interpretation of the primary data in the preparation of the IRIS summary sheets and Toxicological Review for Xylenes.

**Recommendations**

Based on your reading and analysis of the information provided, please identify your overall recommendation for the IRIS materials you have reviewed as:

- acceptable as is
- acceptable with minor revision (as indicated)
- acceptable with major revision (as outlined)
- not acceptable

APPROVAL BY VERSAR, INC.

BY: _____
NAME: David Bottimore
TITLE: Program Manager
DATE: _____