Summary of the Peer Review of the Technical Support Document Titled: Methods to Develop Inhalation Cancer Risk Estimates for Chromium and Nickel Compounds.

Three independent external peer reviewers[1,2,3] were asked to participate in the review of the methods for developing inhalation cancer risk estimates associated with emissions of chromium and nickel compounds from coal- and oil-fired electric utility steam generating units (EGUs) estimates in support of EPA's recently proposed Mercury Air Toxics Rule.[4] The approaches and rationale for the technical and scientific considerations used to derive inhalation cancer risks were summarized in the document titled *Methods to Develop Inhalation Cancer Risk Estimates for Chromium and Nickel Compounds*. A series of charge questions were posed to the peer reviewers in order to determine the technical and scientific relevance of the approaches used to develop the inhalation unit risk estimates which are based on the speciation data available from selected source categories, and on the available unit risk estimates (UREs) reflecting the dose that corresponds to a specific level of cancer risk. This document presents the individual charge questions (chromium and compounds presented first, followed by nickel compounds), a brief summary of the peer reviewers' comments and recommendations, and how those recommendations can be addressed by the EPA in future risk characterizations.

1- <u>Chromium and Compounds</u>

a. **Do EPA's judgments related to speciated chromium emissions adequately take into account the available chromium speciation data?** Two of the reviewers were in agreement with the EPA in that, although the chromium speciation data available are limited, the EPA had both considered appropriately the available data and highlighted the high level of uncertainty associated with these data. The third author also agreed that the chromium speciation database is limited and recommended several additional studies for EPA's consideration. The EPA reviewed these studies and added relevant information from studies of coal-combustion speciation indicating the percentage of hexavalent chromium ranging from below detection limits to levels two fold higher than those reported in past speciation analyses. Thus, the more

[1] Dr. Michael Waalkes, National Toxicology Program, National Institute of Environmental Health Sciences- National Institutes of Health, Research Triangle Park, North Carolina.
[2] Dr. Herman Gibbs, Sciences International Inc., Alexandria, Virginia.
[3] Dr. David Eastmond, Department of Cell Biology and Neuroscience, University of California, Riverside.
[4] US EPA, 2011. National Emission Standards for Hazardous Air Pollutants from Coal- and Oil-fired Electric Utility Steam Generating Units and Standards of Performance for Fossil-Fuel-Fired Electric Utility, Industrial-commercial-Institutional, and Small Industrial-Commercial-Institutional Steam Generating Units Rule. Available online at http://www.epa.gov/ttn/atw/utility/utilitypg.html.

recent speciation data available is unlikely to reduce the uncertainty of the chromium speciation analyses used by EPA as the bases for risk characterization analysis.

b. **Has the EPA selected the species of chromium (i.e., hexavalent chromium) that accurately represents the toxicity of chromium and compounds?** All three authors were in agreement that hexavalent chromium was the best scientifically supported carcinogenic species that represents the toxicity of chromium and compounds.

c. **Are the assumptions used in past analysis scientifically defensible, and are there alternatives that the EPA should consider for future analysis?** Two reviewers considered the assumptions applied (primarily, the assumption that hexavalent chromium constitutes 12 % of the total coal-fired utilities, and 18% of oil-fired utilities, based on the speciation data available) to be reasonable given the limited data available for chromium speciation profiling. Given the limited chromium speciation data available, and the view of the majority of the peer reviewers, the EPA considers it reasonable to use the same approach in future risk analyses. The third reviewer did not comment on the speciation assumptions used in past analysis.

2- <u>Nickel and Compounds</u>

a. **Do EPA's judgments related to speciated nickel emissions adequately take into account available speciation data, including recent industry spectrometry studies?** Two of the reviewers, which are in agreement with the views of the EPA, consider all nickel compounds as carcinogenic, and thus did not focus on nickel speciation or nickel solubility as strong determinants of carcinogenicity. These views are based in agreement of major scientific bodies (i.e., NTP, IARC, WHO) in that the integrated evidence from epidemiological studies, mechanistic studies and carcinogenesis studies in rodents support the concept that nickel compounds should be considered carcinogenic, as a group. Further, with exception of IRIS (which has only derived unit risk estimates for nickel subsulfide and nickel refinery dusts)[5], the other two unit risk estimates derived by California Department of Health Services

[5] IRIS derived URE values for 2 nickel compounds, nickel subsulfide (0.00048 per $\mu g/m^3$) and nickel refinery dust (0.00024 $\mu g/m^3$). The other available UREs that have both been derived for nickel compounds, as a group, are the one developed by the California Department of Health Services (CDHS, 1991) and another by the Texas Commission on Environmental Quality (TCEQ, Development Support Document, 2011) , with values of 0.00026 per $\mu g/m^3$ and 0.00017 $\mu g/m^3$, respectively.

(CDHS, 1991) and the Texas Commission on Environmental Quality (TCEQ, Development Support Document, 2011)[6] have been derived for nickel compounds as a group. The third reviewer recommended that the EPA review several manuscripts that might (directly or indirectly) be relevant to nickel speciation profiling. However, as mentioned above, EPA, in agreement with two out of the three peer reviewers, considers nickel compounds to be carcinogenic as a group.

b. Based on the speciation information available and on what we know about the health effects of nickel and compounds, and taking into account the existing URE values (i.e., values derived for IRIS, Cal EPA and Texas), the EPA has provided several approaches[7] to derive unit risk estimates that may be more scientifically defensible than those used in past analyses. Which of the options presented would result in more accurate and defensible characterization of risks from exposure to nickel and compounds? Are there alternative approaches that the EPA should consider?

Two of the reviewers suggested the consideration of all nickel compounds as carcinogenic, which would lead to using the URE selected without application of a factor. The third reviewer pointed at only considering nickel subsulfide as carcinogenic (which was an approach used by the EPA in past analyses) with the application of a factor that would account for the fraction of nickel subsulfide from total nickel emissions. EPA disagrees with the latter reviewer based on the information discussed above (i.e., the available scientific evidence supports considering all nickel compounds as carcinogenic). The other aspect of this charge question was related to whether the EPA should consider an alternative approach. Two of the reviewers suggested using the URE derived by TCEQ rather than the one derived by Integrated Risk Information System (IRIS). The third author did not comment on alternative approaches. The EPA has decided to continue using the current IRIS URE because IRIS derived values are at the top of our hierarchy with respect to dose response information used in EPA's risk characterization.[8]

[6] Texas Commission on Environmental Quality (TCEQ), 2011. Development Support Document for nickel and inorganic nickel compounds. Available online at http://www.tceq.state.tx.us/assets/public/implementation/tox/dsd/final/june11/nickel_&_compounds.pdf

[7] See section 3.3 of the document titled "Methods to Develop Inhalation Cancer Risk Estimates for Chromium and Nickel Compounds".

[8] Health Effects Information Used in Cancer and Noncancer Risk Characterization

Nevertheless, taking into account that there may be differences in toxicity and/or carcinogenic potential across the different nickel compounds, and given that there have been two URE values derived for exposure to mixtures of nickel compounds that are 2-3 fold lower than the IRIS URE for nickel subsulfide, the EPA also considers it reasonable to use a value that is 50 percent of the IRIS URE for nickel subsulfide for providing an estimate of the lower end of a plausible range of cancer potency values for different mixtures of nickel compounds.

for the 1999 National-Scale Assessment. Available online at http://www.epa.gov/ttn/atw/nata1999/99pdfs/healtheffectsinfo.pdf.