DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

National Institutes of Health
National Institute of
Environmental Health Sciences
P. O. Box 12233
Research Triangle Park, NC 27709

November 2, 2005

Ms. Courtney M. Price
Vice President, CHEMSTAR
American Chemistry Council
1300 Wilson Boulevard
Arlington, Virginia 22209

Re: Naphthalene Information Quality Act Request for Reconsideration submitted February 18, 2005

Dear Ms. Price:

We are responding on behalf of the National Institute for Environmental Health Sciences to your February 18, 2005 Request for Reconsideration (RFR) submitted on behalf of the Naphthalene Panel of the American Chemistry Council (ACC) . The RFR requests correction of information disseminated by the National Toxicology Program (NTP) concerning the Background Document for Naphthalene and the review of scientific data relevant to NTP's consideration of naphthalene for listing in the 11th *Report on Carcinogens* (*RoC*).

In considering your request, we reviewed the NIH and HHS Information Quality Guidelines (http://aspe.hhs.gov/infoquality/Guidelines/NIHinfo2.shtml and http://aspe.hhs.gov/infoquality/Guidelines/index.shtml), the *RoC* Listing Criteria, your April 1, 2004 Request for Correction of Information with all attachments, and the January 18, 2005 response from the NTP. This information was used in determining the merits of your appeal.

Request for Correction of the Background Document

We concluded that there is no evidence of noncompliance with the NIH and HHS Information Quality Guidelines with respect to the NTP's handling of the Background Document for Naphthalene. The reasons for this determination are as follows:

1. The Background Document is meant to be an unbiased compendium of carcinogenicity and toxicology information, including both positive and negative findings, from publicly available, peer-reviewed literature. As stated in the NTP response, "In background documents, the NTP declines to draw conclusions about the data described or include interpretative information and evaluation" since drawing such conclusions would amount to a usurpation of the functions of the review committee members for whom the information in the background documents is intended.
2. As pointed out in the earlier response, the scientists who are members of these review committees are provided with all public comments, generated at multiple points of the review process, to supplement the information contained in the background documents. It has been the NTP's policy decision to publish the original Background Document together with all the

associated public comments, rather than a revision. The principal reason for the existence of any Background Document is to serve as a compilation of information on relevant studies for the use of the scientific reviewers. The NTP clearly articulates in the description of its RoC process that the Background Document will not be changed and that supplemental information, such as public comments, will be distributed to the review committees. The reason for disseminating the Background Document and associated comments is to provide the public with a window on the process by showing what information was considered by the scientific review committees.

3. To the extent that the Background Document on Naphthalene contains statements on the production, exposure, use, and environmental fate of naphthalene that did not include the most recently available information, it should be noted that the additional data and information provided in the ACC's public comments have been incorporated in the Summary Profile portion of the Naphthalene listing in the 11th *RoC*. Therefore, with respect to these statements as well as the other issues raised by the ACC in its comments, it is clearly not true that the NTP has "simply failed to use the best available science" as you charge in your February 18 reconsideration request. In accordance with the published RoC process, the NTP provided all of the ACC's comments and information to the scientific review panels for consideration along with the other information at their disposal.

Request for Correction of the RG1 and RG2 Summary Reports

With respect to the second request made in your Request for Reconsideration regarding the summary reports from the review groups (RG1 and RG2)[1], we conclude that these summaries do, in fact, provide a concise assessment of the primary rationales for the recommendations of the two groups. Specifically, the RG1 report states, in support of its vote of 6 yes to 1 no: "The committee felt that the NTP two-year inhalation study in F344 rats provided strong evidence for the carcinogenicity of naphthalene in that species...The committee agreed that the evidence of carcinogenicity in $B6C3F_1$ mice was less impressive...There was some discussion as to whether the Listing Criteria of increased tumor incidence 'to an unusual degree with regard to incidence, site or type' applied to the NTP naphthalene rat study...Many felt that the observed carcinogenic response in rats was sufficient to justify listing naphthalene as *reasonably anticipated to be a human carcinogen.*"

The synopsis of the discussion found in the RG2 summary report is similar in character: concise, but informative. The RG2 found itself split in its vote and was unable to make a majority recommendation for either listing or not listing naphthalene as *reasonably anticipated to be a human carcinogen.* The reasons for the split votes, as the summary makes clear, were due to differences in how the individuals on the committee interpreted the 2-year inhalation study results within the framework of the listing criteria (there was no disagreement concerning the actual study results). Specifically, as stated in the summary, members who voted against listing did so because they judged that "the results of the mouse study were not sufficient to say it is positive in this species and ... that the nasal tumors observed in the rat study, although rare, were insufficient to meet the criteria for listing in the RoC, without supporting evidence in mice." Members who voted for listing believed that "the results of the inhalation bioassay studies in rats and mice were sufficient." The section of the report covering the discussion of the animal data gives additional information about the study results and the lack of resolution within RG2 about

[1] http://ntp.niehs.nih.gov/ntpweb/index.cfm?objectid=BD126CB0-F1F6-975E-76939DCC0D9C5A9C#N .

whether the data constituted sufficient justification for listing naphthalene under the existing RoC Listing Criteria.

I would also like to let you know that the NTP is currently working to revise its process for review of future nominations to the *RoC* to address guidance provided by the *Final Information Quality Bulletin for Peer Review* from the Office of Management and Budget (70FR2664). The NTP provided an overview of a general process for peer review of NTP publications, including the *RoC* background documents and substance profiles, at the August 18 meeting of the NTP Board of Scientific Counselors.

Request for Correction of the RoC Subcommittee Proceedings

With respect to the third request made in your Request for Reconsideration regarding the conduct of the RoC Subcommittee Meeting of November 19, 2002[1], we conclude that it is an inappropriate request because procedures or proceedings of meetings are not defined as "scientific information" under the NIH or HHS Information Quality Guidelines and are therefore not subject to request for correction under the Guidelines. It is our understanding, from the discussion on Page 8 of the NTP's January 18, 2005 response to the initial request, that the events of the November 19, 2002 RoC Subcommittee meeting have been raised and responded to in other correspondence, and we will not address them here.

In conclusion, upon extensive review of the information provided, we find that with respect to the development and use of the Background Document on Naphthalene and the summaries of the RG1 and RG2 scientific review group meetings on Naphthalene, the NTP is in compliance with the NIH and HHS Information Quality Guidelines.

The NTP is planning to revise the process for review for the *RoC*, as was mentioned at the August 18, 2005 meeting of their Board of Scientific Counselors. The NTP will certainly welcome receiving comments on any proposed changes in the review process.

We thank you for your interest and contribution to the *RoC* process; your input is vital for helping to make the *RoC* as accurate as possible in order to serve the best interests of public health.

Sincerely,

Sheila A. Newton

Sheila A. Newton, Ph.D.
Director
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