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*THIS DOCUMENT DELIVERED ELECTRONICALLY*

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National Toxicology Program, Report on Carcinogens  
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**RE: Comments on NTP Proposed Review Process for the 12th Report on Carcinogens**

Dear Dr. Jameson:

The Styrene Information and Research Center<sup>1</sup> (SIRC) is pleased to submit comments in response to the National Toxicology Program's (NTP's) Request for Public Comment on the Proposed Review Process (hereinafter referred to as "Process") for the 12th Report on Carcinogens (RoC), *71 Fed. Reg. No. 159, 47507 (August 17, 2006)*. Styrene was proposed for evaluation under the 12th RoC based on an International Agency for Research on Cancer (IARC) finding of "limited evidence of carcinogenicity in animals and limited evidence of carcinogenicity in humans," *69 Fed. Reg. No. 97, 28940 (May 17, 2004)*. SIRC submitted comments and provided a substantial body of data to inform NTP's review of styrene, in particular because SIRC strongly believes that the analysis by IARC did not consider key, valid data that would have allowed for less stringent conclusions. Accordingly, SIRC has a compelling interest in, and support for, NTP's efforts to enhance its own carcinogen assessment procedures.

SIRC supports NTP's efforts to improve the RoC process. The proposed process represents a very positive improvement over the past procedures that NTP has followed, and we urge the NTP to adopt these changes. We are confident that these changes will assist NTP in producing an improved RoC.

Nevertheless, we believe a few additional changes in the process could be made for a modest amount of resources that would make a major structural improvement over the procedural changes so far proposed. We have reached this conclusion because we believe that the

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<sup>1</sup> The Styrene Information and Research Center's (SIRC's) mission is to evaluate existing data on potential health effects of styrene, and develop additional data where it is needed. SIRC has gained recognition as a reliable source of information on styrene and helping ensure that regulatory decisions are based on sound science. For more information, visit <http://www.styrene.org>.

proposed procedure still falls short of the best practices followed for similar scientific endeavors, including the NTP itself in its Center for the Evaluation of Risks to Human Reproduction (CERHR) program. We believe these shortcomings undermine the quality, integrity, and accountability of the RoC for those in the general public, the private sector, and other government agencies who depend on it. In short, a well-defined, thorough, and transparent process that is consistent with current Executive Branch guidance and best scientific practice is essential to ensure both sound results and broad acceptance of the RoC. SIRC believes that final implementation of RoC modifications consistent with these goals will be well worth the small extra investment on the part of the NTP.

As a supplement to our recommendations below we have developed a process map and a narrative outline of the RoC procedure. We have used these to illustrate how some of our recommendations might be implemented. We also recommend that similar materials be incorporated into the final NTP process to supplement the text, in order to clarify the procedures for all users. A reduction of unintended ambiguity in the described process should contribute to the smooth implementation of the new process.

There are three themes that underlie our specific recommended changes:

1. In our view, the proposed process does not make adequate use of the scientific expertise available outside of NTP in assessing the carcinogenic hazard of identified compounds. In particular, there are many scientists among the interested public who have in-depth experience with these compounds and who can contribute scientifically to the thoroughness of these reviews. Although the proposed process does offer more opportunities for public participation than the previous process, which we strongly support, we believe that it falls short of the best practices among federal agencies, including the practices incorporated into the NTP's own CERHR process. Full opportunity for these outside scientists to comment will help ensure the quality of the reviews, and this is sufficient justification to incorporate these changes. Moreover, full utilization of the most appropriate expertise would also do much to provide both the appearance and actuality of objectivity and credibility of the NTP reviews.

In our comments below, therefore, we recommend the inclusion of several additional opportunities for public comment. We do not believe that this will impose a large burden on NTP because the number of persons with a strong scientific interest in the review of a particular chemical will be small. We also recommend that NTP respond to public comments at various points in the process. Although this too may appear burdensome, we believe that responding to comments will help to focus and facilitate the scientific discussion and in fact will lead to a more efficient process than if comments are left without any response. For example, the interested members of the public will know that particular issues have been satisfactorily resolved from their individual perspectives or that additional data are needed. Responses need not be lengthy, but should deal with the underlying scientific issues.

2. The RoC classifications play an important role in public health decisions in both the governmental and private spheres. The decisions incorporated in the RoC can have major impacts on which substances are used in our society and how they are used and, as such, can have far-reaching economic impacts on producers, users, and society in general. In our view, the robustness of the RoC reviews, as reflected in the amount of time and effort devoted to the development, and especially the review, of draft assessments, has not been commensurate with the important role that the RoC plays in societal decisions. The proposed process makes

improvements in this regard, but we believe that further enhancements are needed to bring the resources and time devoted to its preparation into balance with the importance of the RoC in society's decision making.

3. The current NTP cancer classification choices are limited to only two ("known human carcinogen", and "reasonably anticipated to be a human carcinogen"). In our view there have been cases where substances may have been mis-classified, perhaps because of a sense by reviewers that a compound did not have strong evidence of carcinogenicity that met the RoC criteria but nevertheless should not receive a "clean bill of health" and therefore needed to be accommodated somehow in the RoC listing. This problem needs to be addressed because it undermines the scientific integrity of the listing process and potentially subjects compounds to unfair, overly conservative, classifications, leading to misinformation for the public and unnecessary impacts on consumers, producers, and society as a whole.

Finally, we recognize that the changes we are suggesting have cost implications for NTP. We believe that if the NTP does not have the resources currently, the NTP should either readjust its own internal budget alignments, or ask Congress for the additional funds, or, alternatively, ask Congress to adjust the Congressional mandate. Since the original statute authorizing the RoC was adopted by Congress, the hazard assessment environment has changed significantly, and the NTP process is now only one of several classification processes. The consequences for U.S. society of an inadequately funded or administered assessment process are too serious for NTP to lead a process that falls short of best practices in the field. In our view, a fully funded best practices program or a change in the Congressional mandate are the only two choices that are in the public interest.

We have the following specific recommendations for improvements in the proposed process:

#### **Make-Up of the Expert Panel**

- NTP should invite members of the public to suggest necessary areas of expertise which the panel members should have. It is important that these panels have memberships that are balanced, well qualified, and tailored to the scientific complexities of the data for the specific compounds being reviewed.
- NTP should publish the names and areas of expertise of the proposed panel members and invite the public to comment, as does the National Academy of Sciences.<sup>2</sup>

#### **The Operation of the Expert Panels**

- NTP should ensure that the composition of the expert panels is adequate for the complex tasks with which they are presented. The areas of expertise needed often differ from one compound to another. We suggest that NTP follow one of two approaches: (1)

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<sup>2</sup> In its "Policy on Committee Composition and Balance and Conflicts of Interest, dated May 12, 2003, the National Academies state: "For committee activities that are subject to the institution's procedures for compliance with the requirements of Section 15 of the Federal Advisory Committee Act ("FACA") (either as a matter of law or of institutional policy), the institution will determine and provide public notice on the institution's web site of the names and brief biographies of individuals that the institution appoints or intends to appoint to serve on the committee. The institution will also determine and provide a reasonable opportunity for the public to comment on such appointments before they are made or, if the institution determines that such prior comment is not practicable, in the period immediately following the appointments." (page 7) [http://www.nationalacademies.org/coi/bi-coi\\_form-0.pdf](http://www.nationalacademies.org/coi/bi-coi_form-0.pdf)

NTP could specify that a separate expert panel for each compound-specific assessment be created (This has been the approach of the CERHR program, and it has worked well), or (2) NTP could create a core panel of reviewers which is appropriately supplemented with *ad hoc* members having expertise tailored to the compound under review (as is done in EPA's Voluntary Children's Chemical Evaluation Program [VCCCEP]). (The latter approach would increase the opportunity for consistent practices across chemicals.)

- NTP should allocate enough time for each panel to prepare for the review. We believe that at least two months is necessary, given the likely schedules of the panel members.
- NTP should post on its website and provide members of the panel copies of the comments received from the public on the initial draft background document, together with NTP's response to these comments, in sufficient time for these comments to be thoroughly reviewed before the face-to-face panel meeting. For this reason, the public should be given an opportunity to comment on the draft document with enough lead time so that their comments can be prepared and then reviewed by NTP prior to asking the members of the expert panel to review the initial draft.
- NTP should provide for sufficient face-to-face meeting time for the panel so that a full discussion of the compound can take place, together with collaborative discussion with interested and knowledgeable members of the public at the meeting.
- NTP should make the public comments available to all subsequent review committees, including the Interagency Scientific Review Group (ISRG), the senior scientists from the NIEHS/NTP staff (NSRG) and the Board of Scientific Counselors (BSC).

### **The Role of the Board of Scientific Counselors (BSC)**

- NTP should publish for comment on the web its draft substance profile and ask for public comments. These comments, together with NTP's response to these comments, should be made available to the BSC at the time that the draft materials are provided.
- NTP should distribute the draft materials to the BSC at least 60 days prior to their meeting, especially if the BSC is being tasked with review of multiple compounds at a given meeting. We believe that 45 days is too short a period of time.
- Based on the remaining issues identified by the public comments on the draft substance profile, the NTP should allocate an adequate amount of time for the review of the draft in its face-to-face meeting. The historical period of one or two hours is likely to be inadequate and too cursory for many of these compounds.
- NTP should more clearly define the role of the BSC in light of the new process that will rely on expert panels to help formulate the draft substance profile. The BSC should, in our view, be focused on resolving outstanding issues raised in the prior reviews and looking for major inconsistencies and/or data omissions or misinterpretations.


- NTP should invite the BSC to comment on the NTP's listing decision as well as the supporting reasoning, contrary to what is stated in the proposed process.
- To maintain the openness of the process and maintain the integrity of the process, NTP should keep all of the BSC meetings open and not resort to closed sessions. We see no reason why any of the discussions of the BSC should be kept secret.
- If in reviewing the BSC's recommendations, NTP concludes that it should revise the proposed RoC in a way that differs from the BSC's recommendations, NTP should give the BSC members an opportunity for further comment for consideration in the remaining review process within the Department.

### **Strict Adherence to the Criteria for Characterization of Carcinogens**

- NTP should strictly adhere to its criteria for placing compounds in each of the two cancer classifications.
- NTP should consider making even more explicit its policy that it is not compiling a list of compounds for which there is some evidence related to carcinogenicity, but rather a list of those compounds that meet the criteria as "known human carcinogens" or those compounds "reasonably anticipated to be carcinogenic to humans." A decision not to list a compound in the RoC should not be interpreted as giving the compound a "clean bill of health."

SIRC very much appreciates the opportunity to provide these suggestions in response to NTP's request for comments on the RoC Process. We would be pleased to discuss these comments in greater detail. Please contact me at the number below if there are any questions regarding this letter. As noted previously, draft suggested formats for a Process Map and a Narrative Outline of the RoC procedure are attached to this letter.

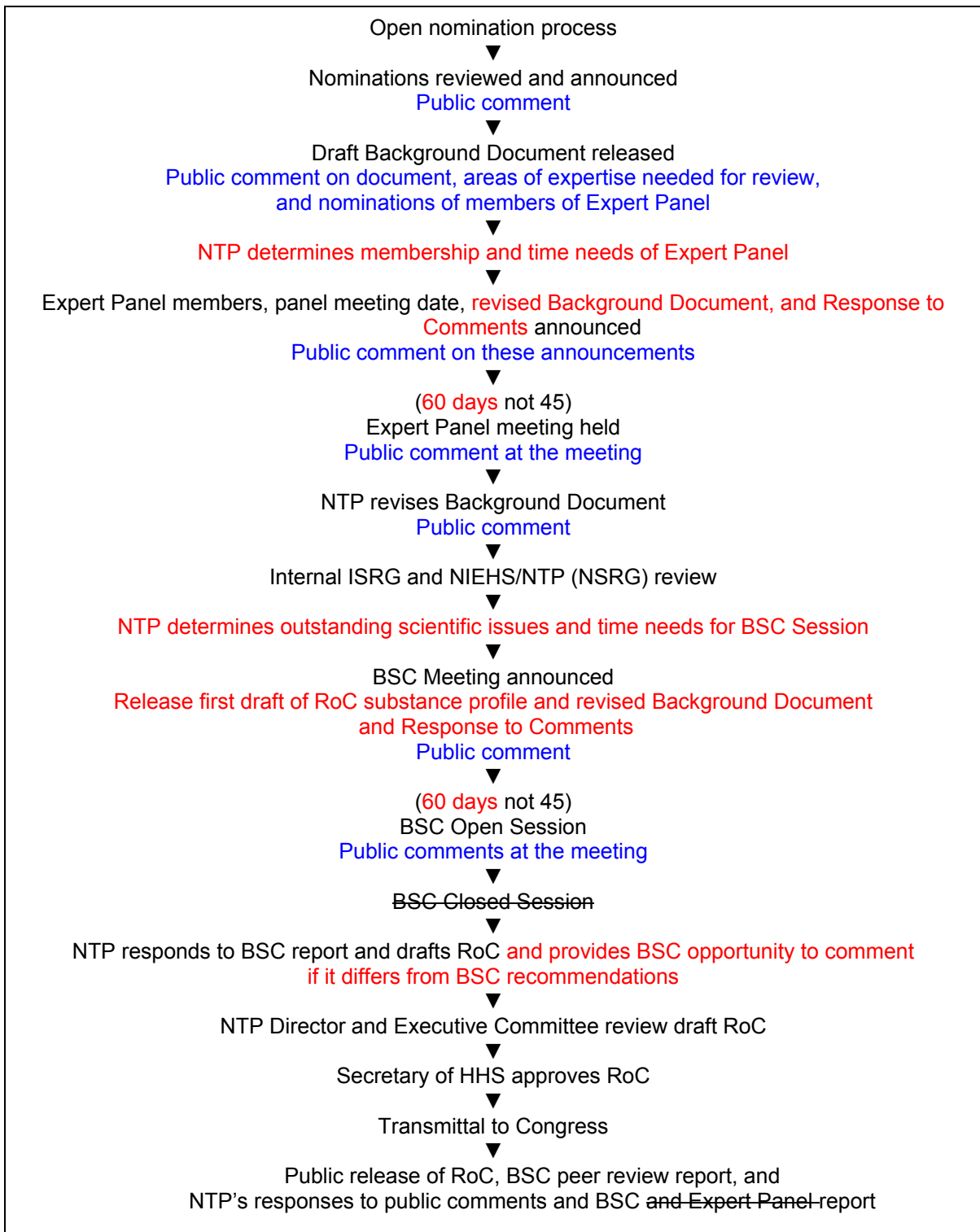
Very truly yours,



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Enclosures

## Suggested Changes to ROC Process Map (See Narrative Outline for details)



Proposed changes in red Times Roman

Strikethrough indicates deletion from NTP proposal

Public comment opportunities in blue

## NARRATIVE OUTLINE OF NTP REPORT ON CARCINOGENS PROCEDURES

SIRC's suggested changes are reflected by the use of a different color and font. ~~Strikethrough~~ indicates deletion of step as specified in the NTP proposal.

1. NTP Invites Nominations to
  - a. List new substance, or
  - b. Reclassify listed substance
2. Initial Staff Evaluation of Nominations
  - a. Justification for nomination or no action prepared
3. NTP announces Nominations
4. Public comment sought via Federal Register notice
  - a. Information on carcinogenicity, current production, exposure, and patterns of use.
  - b. Public nominations for expert panel
5. NTP drafts background document, posts draft on RoC website, announces on NTP listserv **and seeks public comment on document, suggested areas of expertise for the review and nominations for the expert panel**
6. **NTP posts the responses from the public on the RoC website**
7. **NTP reviews comments on document and revises it if appropriate.**
8. **NTP determines membership and time needs of Expert Panel**
9. Expert Panel meeting
  - a. Ad hoc group of public and private sector scientists
  - b. Federal Register notice
    - i. About 45 days prior to meeting date **(SIRC recommends at least 60 days.)**
    - ii. Announces availability of draft background document, **if revised, together with NTP response to public comments**
    - iii. **Announces membership of the expert panel**
    - iv. Public invited to
      1. **Comment on membership of the expert panel and background document.**
      2. Attend
      3. Present oral and/or written comments on draft background document,
      4. Provide opinion on listing status of substance
  - c. All comments, **including those previously submitted**, become part of public record and are reviewed by expert panel
  - d. Panel "is first charged to peer review the background document."
  - e. When the peer review is complete, expert panel asked to:
    - i. Apply the RoC listing criteria to the scientific evidence
    - ii. Recommend listing action
    - iii. Provide scientific justification to support panel recommendation
    - iv. Provide peer review comments on draft background document
10. NTP RoC staff
  - a. **Posts the expert panel report and any new public comments to the RoC website**
  - b. Reviews expert panel and public comments
  - c. Prepares response to peer review report that is made publicly available
  - d. Revises background document, which is posted on RoC website **and invites public comments**

11. Internal review by interagency scientific review group (ISRG) and senior scientists from NIEHS/NTP (NSRG)
  - a. These groups are provided “all relevant information”, including public comments on the revised background document and NTP response to these comments
  - b. They are asked to apply the listing criteria and make a listing recommendation.
12. NTP reviews internal review comments and prepares draft substance profile for the RoC
13. NTP determines outstanding scientific issues and time needs of Board of Scientific Counselors based on Expert Panel report, internal reviews, and public comment.
14. NTP Federal Register notice for Board of Scientific Counselors (BSC)
  - a. Release first draft of RoC substance profile and Background Document if further revised
  - b. Public comments requested, provided to the BSC, and posted on RoC website
  - c. Notice given about 45 days prior to meeting date (SIRC recommends at least 60 days.)
15. Board of Scientific Counselors (BSC) review
  - a. BSC is asked to determine whether the scientific information is correct and supports NTP’s decision; ~~The BSC is not asked to review NTP listing decision as such.~~
  - b. Open session at which public comments are received
  - c. ~~Closed session on draft profiles~~
  - d. BSC prepares and submits a peer review report
16. NTP responds to BSC report and drafts next edition of RoC
17. If new RoC differs from BSC recommendations, NTP provides BSC members an opportunity to provide further comment for consideration in the remaining review process.
18. NTP Director reviews draft RoC
19. NTP Executive Committee reviews and comments on draft RoC
20. Secretary of HHS reviews and approves RoC
21. Final RoC
  - a. Sent to Congress
  - b. Federal Register notice on availability
  - c. BSC peer review report made public
  - d. NTP’s response to BSC report and public comments ~~expert panel~~ posted
  - e. For 12<sup>th</sup> RoC, NTP will prepare response to comments received after posting of final background document (SIRC strongly supports the preparation and posting of NTP’s response to public comments on a routine and on-going basis in order to facilitate and focus the scientific discussion.)

Note: NTP can defer or terminate the review process at any time and will provide public notice of such action.