

September 18, 2006

Dr. C.W. Jameson
National Toxicology Program
Report on Carcinogens
79 Alexander Drive
Building 4401, Room 3118
P.O. Box 12233
Research Triangle Park, NC 27709

Re: Proposed Review Process for the 12th Report on Carcinogens

Dear Dr. Jameson:

The American Chemistry Council is pleased to provide these comments on the National Toxicology Program's new proposed review process for its Report on Carcinogens (RoC).¹ ACC member companies have been active participants in the proceedings that produced most, if not all, of the prior RoCs, acting both individually and through CHEMSTAR panels. This interest had culminated in several instances in Information Quality Act requests for correction of particular RoCs.

ACC itself has also long been engaged in NTP's RoC process, filing correspondence with NTP regarding that process on numerous occasions over the years. Most recently, we supplied NTP with extensive comments on January 30, 2004 in response to the NTP's

¹ 71 Fed. Reg. 47507 (August 17, 2006). The American Chemistry Council (ACC) represents the leading companies engaged in the business of chemistry. ACC members apply the science of chemistry to make innovative products and services that make people's lives better, healthier and safer. ACC is committed to improved environmental, health and safety performance through health and environmental research and product testing, Responsible Care[®], and common sense advocacy designed to address major public policy issues. The business of chemistry is a \$558 billion enterprise and a key element of the nation's economy. It is the nation's largest exporter, accounting for ten cents out of every dollar in U.S. exports. Chemistry companies invest more in research and development than any other business sector. Safety and security have always been primary concerns of ACC members, and they have intensified their efforts, working closely with government agencies to improve security and to defend against any threat to the nation's critical infrastructure. As a science-driven industry, the business of chemistry – through the Council's Long Range Research Initiative and thorough research, screening and testing of specific chemicals by individual member companies – provides significant support for scientific research to better understand and characterize the potential risks from chemical exposures.



Responsible Care[®]

December 2003 request. As can be seen, ACC has had a deep and longstanding concern about the RoC process.

ACC commends NTP for the new proposed RoC process. The new proposal dramatically overhauls the way RoCs will be developed. It is much more reflective of current scientific and administrative practices, as reflected in OMB's Peer Review Bulletin and elsewhere. It also establishes greater consistency between the RoC process and other NTP processes that it increasingly lagged behind – most notably, those of the Center for the Evaluation of Risks to Human Reproduction (CERHR). The new process is particularly refreshing and welcome given the length of time the prior process had endured without significant alteration. NTP deserves great credit for making such a dramatic break with the past by upgrading the RoC process to (i) improve the quality of the scientific analyses and judgments, particularly with respect to evaluating mode of action and the relevancy to human health of results from high-dose studies in animal models; (ii) incorporate opportunities for meaningful consideration of scientific data; and (iii) make the overall analyses and decision-making more transparent.

The new process will greatly increase the scientific and technical quality of the 12th and subsequent RoCs. Early creation of an expert panel, establishment of appropriate opportunities for meaningful public input, and ongoing revision of the resulting work product will all combine to ensure that the best and most relevant information and perspectives are brought into the process at times when they can make a difference. The final report will benefit accordingly.

ACC does have several concerns about the proposal, principally as regards the meetings of the Board of Scientific Counselors (BSC). We also have several other recommendations to improve the proposed process.

Below, ACC summarizes our points of support for the new process, as well as our concerns and recommendations, in the order in the process is discussed on the NTP's website. We, and our members, look forward to working with the NTP as it implements that process for the 12th RoC.

Public Nominations

ACC supports the new process of having a web-based, "Provide Input to NTP" mechanism by which any person can nominate a substance for listing or reclassification² and supply supporting materials. We also support the proposal that, in the event NTP does not proceed with the nomination, NTP will notify the nominating person and invite him or her to submit additional information.

² ACC understands "reclassification," as NTP uses that term, to include delisting a substance. But we urge NTP to clarify that point.

Public Comment on Proposed Substances

ACC also supports NTP's proposal to allow the public to comment on the substances proposed for listing, and to nominate scientists to serve on an expert panel. Companies who make or use a substance are typically aware of who the leading scientific experts are with respect to that substance, and it is important for NTP to have that information.

Expert Panel

Perhaps the single most important aspect of the new proposal is the convening of an expert panel to review the draft background document in a public process. This is one of the greatest strengths of the current CERHR process. By contrast, one of the greatest flaws of the prior RoC process was the absence of formal, outside expert input and review of the background document before its submission to the BSC. Under the new process, experts from the public and private sectors will be able to review the draft at the outset of the process, where any shortcomings or missing data or interpretations can be identified early on and addressed appropriately.

ACC particularly supports NTP's proposals to:

- *Involve scientific experts from the private sector.* For many substances, that is where some of the most knowledgeable experts work.
- *Make the draft background document public much farther in advance of the expert panel meeting.* Historically, background documents have not been made available until only a few weeks, or even less, before the BSC meeting. Generating high-quality work product that will materially assist the expert panel (and NTP) takes more time than that. Although "approximately 45 days" before the meeting would seem to be a much more workable time frame, it is still too short to (i) allow stakeholders to conduct a meaningful scientific review and to develop and submit comments; and (ii) provide an adequate period for the expert panel to review the comments before the meeting. We believe that NTP should establish a 60-day time period as the absolute minimum and make this an obligatory tenet of the RoC program. Any lesser time will undermine the capability of stakeholders to develop and provide meaningful scientific/technical comments and diminish the capability of the expert panelists to fully review and thoroughly reflect on such comments in advance of the meeting.
- *Invite public comment and make those comments available to the expert panel.* This ensures that the expert panel has before it the best and most comprehensive information that it can. NTP should also specify that expert panel meetings be structured in such a way that public commenters have an adequate opportunity to make a presentation and members of the panel have sufficient time to ask questions of the commenters. The meetings should be structured to permit

meaningful public comment and not simply perfunctory public remarks. We suggest that a minimum period of time, on the order of 90 minutes, be built into each meeting for public comment and questions/answers.

- *Create an expert panel report.* The report should clearly address all relevant public comments.
- *Invite public comment on the expert panel report.*
- *Prepare a response to the expert panel's report.* One of OMB's three proposed reforms to the NTP process was some sort of response-to-comments document.³ This is particularly important step, as it assures that the decision-making of NTP is fully transparent to all stakeholders. In addition, this action provides an opportunity for NTP to clearly communicate the program's scientific rationale and justification for (i) accepting or rejecting certain hypotheses; (ii) addressing disparities in datasets; and (iii) arriving at science and policy decisions. Importantly, this response should address not only the expert panel's report but also public comments submitted on it.
- *Revise the background document in light of the expert panel's report and the public's comments.* Another prime flaw in the prior RoC process was the fact that the background document never underwent revision at any of the multiple stages of the process, thus perpetuating whatever shortcomings its admittedly early form contained. Another of OMB's proposed reforms was for the background document to be updated to reflect input received before a final listing decision was made. NTP's new process adopts that recommendation.

In addition, ACC recommends that NTP specify the charge to the expert panel, which should include a review of:

- the proposed mode of action; and
- the weight of the evidence with respect to the carcinogenic potential of the substance to humans.

Finally, ACC also recommends that NTP establish clearly the permissible roles and responsibilities of expert panel members (and BSC members) vs. public commenters. In at least one prior instance, a BSC member who was chairing one of its meetings temporarily assigned his chairman responsibilities to another BSC member, and then proceeded to make a presentation to the BSC regarding a chemical under discussion, providing the BSC members (but no one else), on the spot, with significantly new but apparently unpublished information regarding the chemical. He then resumed his role as chair. This sort of activity by an expert panel member (or a BSC member) should be expressly forbidden. NTP should adopt policies and procedures for both the expert panel

³ Letter dated Nov. 16, 2004 from John Graham to Elias Zerhouni.

meetings and the BSC meetings that clearly describe the roles and responsibilities of expert panel and BSC members.

BSC Public Meeting to Review Draft Profile

The new process proposes that a draft substance profile will be released in advance of the BSC's consideration of it, with public comment invited to be submitted at a public meeting of the BSC. ACC supports this approach. However, ACC recommends that NTP:

- *Provide the BSC with NTP's own response to the expert panel's peer review report.* It is important that the BSC understand how NTP reacts to the substantive points made in that report. That scientific and technical dialogue will enhance the BSC's ability to further the discussion.
- *Specify the number of days in advance of the public meeting that the draft will be provided to the BSC and the public.* It is important that all concerned have an adequate opportunity to review the draft and that the public have enough time to develop comments that will be useful to the BSC. Lack of time was historically a problem with the prior process – commenters were often given a few weeks or less to develop comments, and BSC members virtually no time (only a few hours) to review those comments. As we explained above in connection with the draft background document, we do not believe 45 days is sufficient time for members of the public to review and develop comments on a draft substance profile, and for BSC members to review those comments prior to their public meeting. Rather, we believe a 60-day time period should be the absolute minimum and that this should be made an obligatory tenet of the RoC program.
- *Ensure that the BSC meetings are structured so that members of the public have an adequate opportunity to speak and BSC members sufficient time to ask them questions.* BSC meetings generally cover so many chemicals (a dozen or more) that prior practices have not allowed for meaningful public input or discussion of that input. Five minutes is not enough time for a substantive presentation of the issues raised in the average proposed listing. ACC trusts that the new process will correct that shortcoming by providing something like 15 minutes for presentations and 5 to 10 minutes for BSC members to question each presenter.
- *Establish the same clarity regarding roles and responsibilities for BSC members vs. commenters that we recommended in connection with expert panel meetings.* As noted above, the problematic behavior occurred at a BSC public meeting.

BSC Peer Review Meeting

The last of OMB's recommendations was that NTP conduct a peer review, "perhaps by the [BSC]," of the draft substance profile. NTP has adopted that recommendation and ACC supports it. Having the BSC meet after the public comment session, as an expert peer review panel, reinforces our call for the process to include adequate time to fully

consider the merits of each proposed listing in light of the comments, both written and oral, filed on it. The preparation of a BSC peer review report should also help provide NTP with additional clear scientific guidance as it makes its final listing decision.

ACC is concerned, however, about NTP's use of the phrase "in closed session" to describe this BSC peer review meeting. Historically, BSC meetings have always been open to public observation, even if public participation has been limited. Also, as an advisory committee chartered under the Federal Advisory Committee Act, the BSC is required to hold its meetings in public unless the Secretary of HHS determines to close those meetings for a reason authorized by the Government in the Sunshine Act.⁴ None of those reasons should apply here, and we trust that NTP will continue to conduct all portions of BSC meetings in public session.

ACC is also troubled by the proposal's statement that "[t]he BSC is not asked to review the NTP's decision regarding listing status." Historically, the BSC has been asked for its opinion on such proposed decisions, and this practice should continue. To be clear, the BSC's opinions cannot bind NTP, which has its own statutory obligation to make listing decisions. But BSC's recommendations have proven valuable to NTP in the past, and NTP should not deprive itself of that guidance. NTP is already asking the BSC to opine on "whether the scientific information cited in the draft substance profile for a candidate substance . . . supports the NTP's decision regarding its listing in the RoC." It is only a small further step (or maybe no additional step at all) to ask the BSC to say whether it thinks that decision is correct.

In addition, and as with the expert panel, the charge to the BSC should also include a review of:

- the proposed mode of action; and
- the weight of the evidence with respect to the carcinogenic potential of the substance to humans.

⁴ See 5 U.S.C. App. 2, § 10(d).

Dr. C.W. Jameson
September 18, 2006
Page 7

* * *

NTP has introduced truly fundamental reform to its NTP process, and ACC commends it for doing so. We look forward to working with NTP as it implements the new process. If you have any questions regarding these comments, please contact Rick Becker at 703-741-5210.

Sincerely,

Michael P. Walls
Managing Director
Regulatory & Technical Affairs