



Styrene Information and Research Center (SIRC)

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Dr. Linda S. Birnbaum
Director
National Institute of Environmental Health Sciences / National Toxicology Program
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Re: NAS Formaldehyde Report Supports SIRC Concerns with Deficiencies of NTP Report on Carcinogens Process

Dear Dr. Birnbaum:

As the chairperson of the Styrene Information and Research Center's (SIRC's)¹ Science and Technology Task Group, I write to discuss the critical and direct relevance of the National Academy of Science's (NAS's) April 8, 2011, report on formaldehyde² to the National Toxicology Program's (NTP's) proposal to list the chemical styrene as "reasonably anticipated to be a human carcinogen" in the NTP 12th *Report on Carcinogens (RoC)*.

The NAS report outlines a definitive approach on how hazard identification should be conducted by federal agencies, using a clear and systematic methodology – a methodology that neither EPA's IRIS nor NTP's *RoC* programs have followed in their reviews (and yet, as the NAS reports, is employed by NTP's Center for the Evaluation of Risks to Human Reproduction). The report states that EPA followed a flawed and biased analytic process and did not use the best available scientific data for formaldehyde. NTP reached the same flawed conclusions as EPA on formaldehyde. The NTP also did not use the NAS's recommended process for styrene. **In short, the NAS – the nation's highest scientific body -- identifies and ratifies the serious procedural deficiencies that the styrene industry has cited repeatedly about NTP's *RoC*, as follows:**

- The NAS faults EPA for not having an underlying conceptual framework for its review, despite EPA's publication of hundreds of pages of specific guidelines for how the Agency will conduct these assessments. NTP doesn't have any detailed and publicly-available guidelines for how it conducts its *RoC* assessments, and in the one case where

¹ 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>.

² "Review of the Environmental Protection Agency's Draft IRIS Assessment of Formaldehyde." The Committee to Review EPA's Draft IRIS Assessment of Formaldehyde operated under the National Research Council of the National Academies. The report is available at www.nap.edu/catalog/13142.html

it has a general rule – namely to use only peer-reviewed evidence to make its decisions – the staff violated that rule at least twice for styrene.

- The NAS lays out a requirement for a careful, step-by-step, measured approach to identifying all the relevant literature to be reviewed. However, in the case of styrene, in the final stages of its assessment the NTP ignored a large body of additional and essential studies. These studies were not considered as part of the basis for NTP's final decision making.
- The NAS directs EPA to clearly articulate the criteria by which the Agency chooses to exclude or include a study as a key data point, and to provide a clear description of the weight-of-evidence approaches it uses in order to ensure consistency of treatment of data. Despite the fact that the NTP program is older than EPA's risk assessment program, NTP has articulated no such criteria and instead applies an *ad-hoc* approach to its choice of key studies. Further, NTP uses the selective 'strength-of-evidence' assessment approach, rather than the inclusive 'weight-of-evidence' method of assembling and presenting the scientific evidence for decision makers.
- The NAS report lists criteria for determining causality and a hierarchical system for evaluating the strength of causal inferences based on available data. The NTP did not follow this approach in its review of styrene.

As you know, SIRC for three years has provided strong scientific evidence to your office that the collective database does not support listing styrene in the RoC, and SIRC has vigorously protested the highly deficient scientific process NTP has applied in assessing the carcinogenic potential of styrene for the 12th RoC. As fellow scientists, my colleagues and I likewise have directly communicated to you our professional concerns with NTP's willingness to ignore the standards of robust hazard assessment that are embraced by the larger scientific community – and which now have been clearly defined by the NAS. NTP instead has chosen to support its proposed listing of styrene based on the selective citation of data, including re-assessments of published data that have not been peer reviewed. NTP likewise has ignored cutting-edge research on mouse lung tumor mode of action that is *based on NTP-funded research initiatives*, and which now provides clear evidence that NTP's citation of cancer in mice is not relevant to a human carcinogen concern. In the case of styrene, our opinions on the RoC's process deficiencies definitively are supported by the recent robust, transparent, and independent panel assessments repeatedly cited to you and your staff – namely the European Union styrene assessment and the Boffetta *et al.* epidemiology review – that both reached the conclusion that styrene is not a human carcinogen concern.

And while the economic effects of scientific determinations are not the purview of scientists, it nonetheless is incumbent upon us to ensure that any scientific conclusions that may have economic impacts are based on the most thorough, transparent, and balanced assessments possible. To date, it is clear that has not been the case with NTP's treatment of styrene for the RoC, which indeed will have profound negative impact on society and industry with no commensurate public health benefit.

Therefore, on behalf of SIRC's member scientists, I ask that, in order to be scientifically rigorous as well as both prudent and cautious, you and your staff defer styrene's review from the 12th RoC to the 13th RoC because:

- It will take time to appropriately adopt the hazard assessment principles identified in the NAS report and apply them to current and future RoC reviews;
- Styrene is the first major industrial chemical to be reviewed under the RoC process that was updated before the 12th RoC reviews were conducted, and as such, is precedent-setting for future reviews of other substances; and

- The styrene review, which largely was carried out before your appointment at NIEHS, was, from all appearances, not carried out in full conformance with the principles outlined by NAS.

By deferring styrene's review to the 13th RoC, NTP can, under your personal guidance, conduct a scientifically robust assessment of styrene that carefully applies the hazard assessment procedures recommended by the NAS.

I ask that this letter be added to the styrene docket for the 12th RoC, as part of SIRC's public communications to NTP on this matter.

Very truly yours,

signature redaction

Marcy Banton, DVM, PhD, DABVT
LyondellBasell Corporate HSE/Product Safety
Chairperson
SIRC Science & Technology Task Group

cc:
Dr. Ruth Lunn / NTP